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Some calculations of the activation energies for inversion of diphenyl and a number of *ortho*-halogenated diphenyls. By K. E. HOWLETT

745. *Polynucleotides. Part II.*[1] *Homopolymers of Cytidylic and Pseudouridylic Acid, Copolymers with Repeating Subunits, and the Stepwise Synthesis of Polyribonucleotides.*

By A. M. Michelson.

Cytidylic and pseudouridylic acid have been polymerised by the action of diphenyl phosphorochloridate. The properties of the polymers are in accord with those of polyadenylic, polyguanylic, and polyuridylic acid previously reported. A definitive preparation of glycol cyclic phosphates using ethyl chloroformate in aqueous solution is described. Oligonucleotides with a defined order of bases have been prepared by polymerisation of three dinucleotides and a trinucleotide isolated as pure solids from a ribonuclease digest of yeast ribonucleic acid. A number of dinucleoside phosphates have been synthesised in good yield by treatment of a 2′,3′-di-*O*-acetyl-nucleoside and a 5′-*O*-acetyl-nucleoside-2′,3′ cyclic phosphate with diphenyl phosphorochloridate and base. By further stepwise addition of nucleotide, five oligonucleotides containing three different bases and six containing four different bases have been prepared. The physical properties of these compounds confirm a restricted rotation about the internucleotide linkage even in small oligonucleotides.

In Part I[1] was described the synthesis of a number of polynucleotides by the action of diphenyl phosphorochloridate on the nucleoside-2′(or 3′) phosphate. Extension to the polymerisation of pseudouridylic acid[2] was straightforward, giving polypseudouridylic acids of different chain lengths. However, initial approaches to the polymerisation of cytidylic acid indicated that protection of the amino-group was necessary. While treatment of cytidine-2′,3′ cyclic phosphate with diphenyl phosphorochloridate in the usual way gave polymers, as shown by paper chromatography and dialysis of the products, these products were stable to treatment with mild acid or alkali and were unaffected by ribonuclease or the mixture of enzymes present in rattlesnake venom. Further, the ultraviolet absorption spectra in acid and alkali were virtually identical, whereas cytidylic acid shows a characteristic change due to ionisation of the amino-group. It is likely therefore that a large part of this material contained internucleotide linkages from the 2′- or 3′-phosphate to the 6-amino-group of the pyrimidine ring. Attention was therefore directed to selective acetylation of this amino-group. Cytidine-2′,3′ cyclic phosphate with 1 mol. of acetic anhydride gave a 95% yield of the required N^6-acetylcytidine-2′,3′ cyclic phosphate with only traces of unchanged material and $N^6O^{5'}$-diacetylcytidine-2′,3′ cyclic phosphate. The monoacetylated material was not a mixture of N^6- and *O*-acetyl derivatives because the ultraviolet absorption spectra in acid and neutral solution were identical with those of $N^6O^{5'}$-diacetylcytidine-2′,3′ cyclic phosphate (Fig. 1) and showed completely the changes previously[3] noted as characteristic of acylation of the amino-group of cytosine nucleosides. Preliminary experiments indicated that the amino-acetyl group was readily removed by very mild treatment with alkali (pH 9·6) (this also partially hydrolysed the cyclic phosphate to 2′- and 3′-phosphates), while spectral studies of the compound in 0·04N-sodium hydroxide at room temperature showed 80% deacetylation in 10 min. and complete deacetylation in 30 min.

Treatment of N^6-acetylcytidine-2′,3′ cyclic phosphate with diphenyl phosphorochloridate, followed by removal of the acetyl group, gave polycytidylic acid in good yield.

The properties of polypseudouridylic and polycytidylic acid were in general agreement with those of the homopolymers of adenylic, guanylic, and uridylic acid.[1] Alkali-treatment gave a mixture of the 2′- and the 3′-phosphates; crude rattlesnake venom degraded

[1] Part I, *J.*, 1959, 1371.
[2] Cohn, *Biochim. Biophys. Acta*, 1959, **32**, 569.
[3] Michelson and Todd, *J.*, 1954, 34.

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the polymers to nucleoside and nucleoside-2′(3′),5′ diphosphate, and ribonuclease effected partial breakdown to the mononucleotide and a series of oligonucleotides containing 2′–5′-linkages exclusively. Although polypseudouridylic acid had very slight effect on the absorption spectra of Toluidine Blue and Acridine Orange, the action of polycytidylic acid was more pronounced. The influence of chain length on this interaction with dyes is

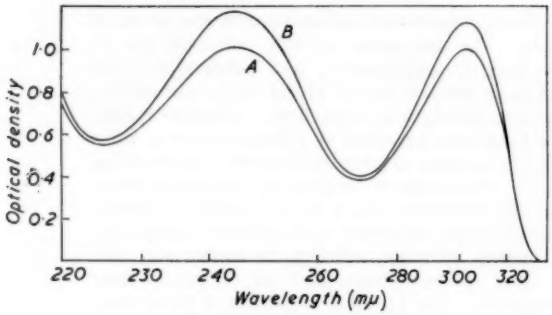


FIG. 1. *N^6-Acetylcytidine-2′,3′ cyclic phosphate (A) and $N^6O^{5'}$-diacetylcytidine-2′,3′ cyclic phosphate (B) in* 0·01N-HCl.

indicated in Fig. 3; minimum chain lengths of 8—10 nucleotides would seem to be necessary for significant interaction.

Some optical properties of the polymers are given in Table 1. Comparison of the hyperchromic effects shown by the homopolymers and by various dinucleoside phosphates shows that the generalisation that "the diminution in $\varepsilon_{max.}$ for the purine containing compounds is considerably higher than that for the compounds containing only pyrimidines" [4] is not valid. The small hypochromic values for apurinic acid are probably due, not

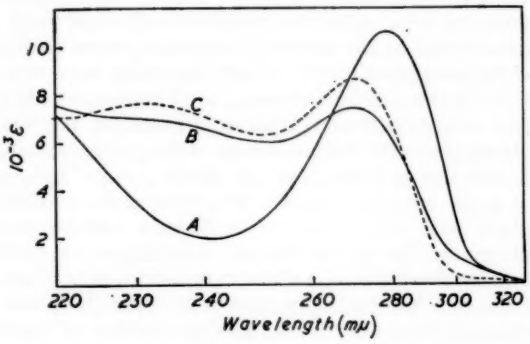


FIG. 2. *Polycytidylic acid (average chain length* ca. 10 *units). A, in* 0·01N-HCl; *B, in* 0·1N-NaOH; *C, alkaline hydrolysis products in* 0·1N-NaOH.

so much to removal of purines, as to dilution of the effect due to tracts of two, three, or more pyrimidines by single pyrimidines flanked by deoxyribose units (effectively mononucleotide material).

Like yeast ribonucleic acid, all the synthetic homopolymers (and copolymers) gave precipitates with protamine sulphate in neutral aqueous solution. These precipitates were partially soluble in 2M-sodium (or lithium) chloride, but were reprecipitated on dilution to an ionic strength of 0·2M or less.

Dr. K. S. Kirby, of the Chester Beatty Institute, has examined the countercurrent distribution of the homopolymers of adenylic, cytidylic, guanylic, and uridylic acid (all of average chain length ~6) and of an improved preparation of poly ACGU. The results

[4] Gilham and Khorana, *J. Amer. Chem. Soc.*, 1958, **80**, 6212.

are shown in Fig. 4. An indication of partial interaction between polycytidylic acid and polyguanylic acid was observed. Paper electrophoresis also indicated partial interaction, but only a slight decrease in absorbance (3%) occurred when solutions of the two polymers were mixed. Since no interaction occurred between the synthetic polyadenylic and polyuridylic acid, it may be concluded that hydrogen bonds between the cytosine 6-amino-groups and guanine NH·CO groups are stronger than those between adenine and uracil.

TABLE 1. *Ultraviolet spectra.*

	In 0·01N-HCl		In 0·1N-NaOH		Alkaline hyperchromicity (%)
	$\lambda_{max.}$ (mμ)	$\lambda_{min.}$ (mμ)	$\lambda_{max.}$ (mμ)	$\lambda_{min.}$ (mμ)	
Dicytidylic	278	240	270	250	8·7
Tricytidylic	278	241	270	251	13·9
Tetracytidylic	278	241	270	251	15·3
C2′P5′CP	278	241	270	251	11·0
C2′P5′C2′P5′CP	278	241	270	251	15·7
Polycytidylic (4·4)	278	241	270	251	13·9
Polycytidylic (9·8)	278	241	270	251	15·9
Polypseudouridylic (6·2)	262	231	285	246	10·5
" Stable " polycytidylic	273	244	273	246	0

Various workers [5] have used cellulose anion-exchange materials for fractionation of polynucleotides. The use of " Ecteola " cellulose (Brown Co., Berlin, New Hampshire) for fractionation of nucleotides of low molecular weight is demonstrated by the ready separation of adenosine-2′,3′ cyclic phosphate, adenosine-2′ phosphate, and adenosine-3′ phosphate at neutral pH by gradient elution with aqueous lithium chloride (Fig. 5). Representative chromatographic analyses of synthetic polyuridylic and polyguanylic acids (before dialysis) are shown in Fig. 6. Similar elution diagrams were obtained for the other homopolymers.

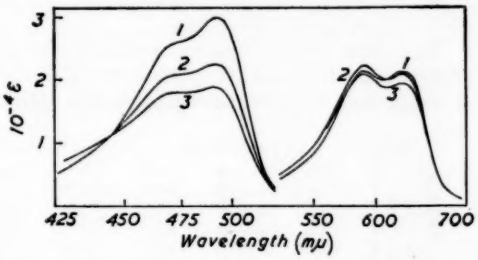


FIG. 3. *Action of polycytidylic acid* [3 × 10^{-5}M (P)] *on the absorption spectra of Acridine Orange* (3 × 10^{-5}M) (*left*) *and Toluidine Blue* (3 × 10^{-5}M) (*right*) *in* 0·01M-*ammonium acetate at* pH 6·8. 1, *Dye alone*; 2, *and* 3, *with added polycytidylic acid of average chain length* ~6 *and* ~10 *nucleotides respectively.*

As part of a programme directed to the polymerisation of nucleotides in aqueous solution the use of ethyl chloroformate as a cyclising agent has been examined. In view of the general solvent difficulties in this field it is of particular interest that quantitative yields of all the nucleoside-2′,3′ cyclic phosphates (and of glycerol-1,2 cyclic phosphate and glycol-1,2 cyclic phosphate) were obtained by treating the appropriate phosphate with ethyl chloroformate and base in *aqueous* solution. The reagent was also effective in anhydrous media.

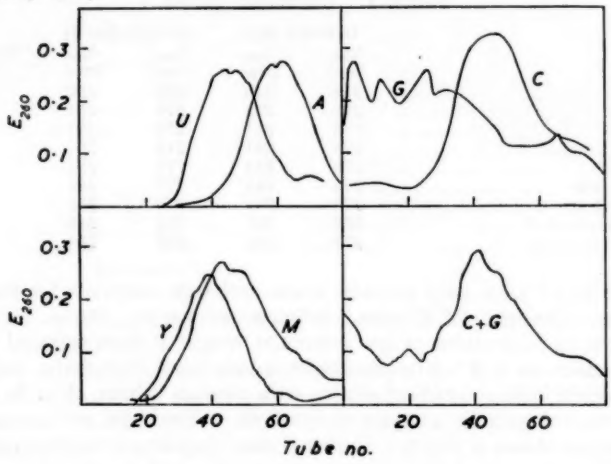
Enzymic degradation of ribonucleic acid to oligonucleotides ending with a pyrimidine nucleoside-3′ phosphate, the remainder of the molecule consisting of purine nucleotides, provides a convenient preparation of small polynucleotides of defined structure. Volkin and Cohn described [6] the fractionation of such mixtures using Dowex anion-exchange resin. By repeating this work on a large scale, 5′-(3′-adenylyl)cytidine-3′ phosphate,

[5] Bendich, Fresco, Rosenkranz, and Beiser, *J. Amer. Chem. Soc.*, 1955, **77**, 3671; Bendich, Pahl, Korngold, Rosenkranz, and Fresco, *J. Amer. Chem. Soc.*, 1958, **80**, 3949; Bradley and Rich, *ibid.*, 1956, **78**, 5898; Tener, Khorana, Markham, and Pol, *ibid.*, 1958, 80, 6223.

[6] Volkin and Cohn, *J. Biol. Chem.*, 1953, **205**, 767.

5′-(3′-guanylyl)cytidine-3′ phosphate, 5′-(3′-adenylyl)uridine-3′ phosphate, and 5′-[5′-(3′-adenylyl)-3′-adenylyl]cytidine-3′ phosphate (*i.e.*, A3′P5′A3′P5′C3′P) were obtained as pure solids and characterised by the usual methods.[6] While the dinucleotides were inert to the enzymes in rattlesnake (*Crotalus atrox*) venom, the trinucleotide was slowly hydrolysed

FIG. 4. *Countercurrent distribution of polyadenylic (A), polycytidylic (C), polyguanylic (G), polyuridylic (U), poly ACGU (M), and yeast ribonucleic (Y) acids, and of a mixture of polycytidylic and polyguanylic acids (C + G).*



to adenosine, cytidine-3′,5′ diphosphate, and a trace of dinucleotide [presumably 5′-(3′-adenylyl)cytidine-3′ phosphate].

Treatment of these oligonucleotides under suitable conditions with ethyl chloroformate converted the terminal phosphate into a 2′,3′-cyclic phosphate with only slight degradation to compounds of lower molecular weight. Reaction of 5′-[2′(or 3′)-adenylyl]uridine-2′,3′

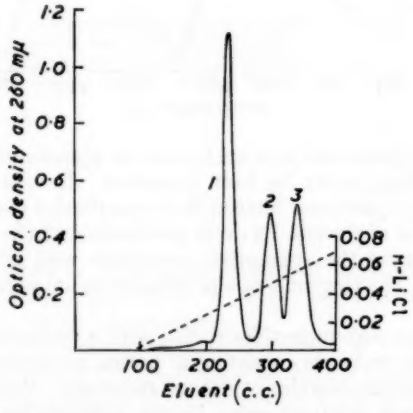


FIG. 5. *Fractionation of adenosine-2′,3′ cyclic phosphate* (1), *adenosine-2′ phosphate* (2), *and adenosine-3′ phosphate* (3) *on an* "Ecteola" *cellulose column* (10 × 1 cm.) *with gradient elution with aqueous lithium chloride. Flow rate* ~1 c.c./min.

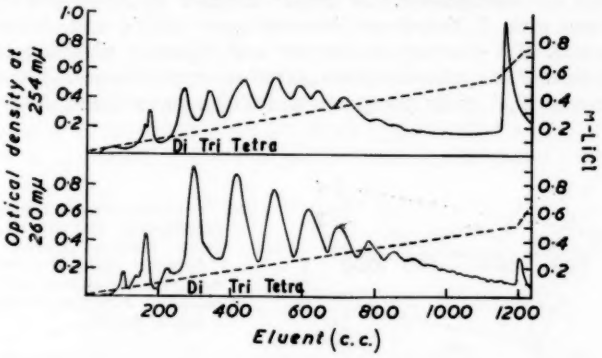
cyclic phosphate with diphenyl phosphorochloridate and tri-n-butylamine in anhydrous solution gave a series of polymers containing 2, 4, 6, etc., nucleotides, again with only slight apparent cleavage of the original internucleotide linkage. With cytosine-containing polynucleotides, the 6-amino-group was selectively acetylated after cyclisation of the terminal phosphate, and the protected compound was then polymerised, acetyl groups

being removed from the product by mild alkali-treatment. Optical properties of the oligonucleotides are given in Table 2.

A shift in the apparent pK_a's (spectrophotometrically determined) of 5'-(3'-guanylyl)-cytidine-3' phosphate to 4·45 (280 mμ) and 10·2 (265 mμ) was observed on polymerisation of the dinucleotide. This type of shift has been noted previously [7] for a number of deoxynucleic acids.

The polymers showed the expected behaviour towards alkali and rattlesnake venom.

FIG. 6. *Chromatographic analysis of polyguanylic acid (upper curve) and polyuridylic acid (lower curve) (before dialysis) on an "* Ecteola *" cellulose column* (12 × 1 cm.) *with gradient elution with aqueous lithium chloride. Flow rate* ~1 c.c./min. *Approx.* 10 mg. *of polymer.*



Pancreatic ribonuclease released no mononucleotide, but did not cause complete breakdown to the original oligonucleotide owing to the presence of 2'–5'-linkages. While no evidence is available at the moment, the original 3'–5' purine–pyrimidine linkages were presumably partially isomerised during polymerisation.

TABLE 2. *Optical properties.*

Compound	In 0·01N-HCl $\lambda_{max.}$ (mμ)	In 0·01N-HCl $\lambda_{min.}$ (mμ)	In 0·01N-HCl 280/260 mμ	In 0·1N-NaOH $\lambda_{max.}$ (mμ)	In 0·1N-NaOH $\lambda_{min.}$ (mμ)	In 0·1N-NaOH 280/260 mμ	Alkaline hyperchromicity (%)
A3'P5'A3'P5'C3'P	259	232	0·52	259	229	0·36	22·5
A3'P5'A3'P5'C	259	232	0·53	259	230	0·39	23·3
A3'P5'A	257	230	0·22	258	229	0·19	10·7
A3'P5'C3'P	265	234	0·75	260	229	0·41	8·0
A3'P5'C	265	234	0·76	261	230	0·44	7·6
G3'P5'C3'P	276	233	1·10	268	231	0·70	3·8
G3'P5'C	276	233	1·25	268	232	0·76	3·0
A3'P5'U3'P	258	230	0·26	259	233	0·20	4·1
A3'P5'U	257	230	0·30	259	233	0·23	1·4
Poly (AAC) 2M-NaCl residue	260	233	0·54	259	229	0·43	28·8
Poly (AU) 2M-NaCl residue	260	235	0·26	259	237	0·24	17·2
GPCPGPCP	273	235	1·17	267	235	0·70	3·1

As shown by chromatography on " Ecteola " cellulose (Fig. 7) polymerisation was not so effective as with the mononucleotides. Indeed, with 5'-(3'-guanylyl) cytidine-3' phosphate the major product was the tetranucleotide, with unchanged material and small amounts of the hexanucleotide.

Three types of nucleotide co-polymer (random A and B, tracts of A and B, and alternating A and B) have been described. The next stage of the work concerned the stepwise synthesis of a number of oligonucleotides containing up to four different bases in a defined order. Although, partly for historical reasons, further addition has not been attempted,

[7] Lee and Peacocke, *J.*, 1951, 3361.

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extension to the stepwise synthesis of higher oligonucleotides may be expected to offer little difficulty.

Adenosine-2′(or 3′) phosphate was converted into the cyclic phosphate by the action of ethyl chloroformate and base in aqueous solution. The anhydrous tri-n-butylammonium salt was then acetylated to give 5′-*O*-acetyladenosine-2′,3′ cyclic phosphate; under the conditions employed the N^6-acetyl derivative was not obtained, as shown by ultraviolet absorption spectra of the product. Addition of diphenyl phosphorochloridate and base to a mixture of this protected nucleotide and 2′,3′-di-*O*-acetyluridine in anhydrous solution gave a good yield of the protected dinucleoside phosphate from which acetyl groups were removed with mild alkali, to give a mixture of 5′-(2′- and 3′-adenylyl)uridine, separated by ion-exchange chromatography. A similar reaction of N^6-$O^{5'}$-diacetylcytidine-2′,3′ cyclic phosphate with 2′,3′-di-*O*-acetyluridine gave 5′-(2′- and 3′-cytidylyl)uridine, while treatment of 2′,3′-di-*O*-acetyladenosine and diphenyl phosphorochloridate with 5′-*O*-acetyladenosine-2′,3′ cyclic phosphate, $N^6O^{5'}$-diacetylcytidine-2′,3′ cyclic phosphate, 5′-*O*-acetylguanosine-2′,3′ cyclic phosphate and 5′-*O*-acetyluridine-2′,3′ cyclic phosphate

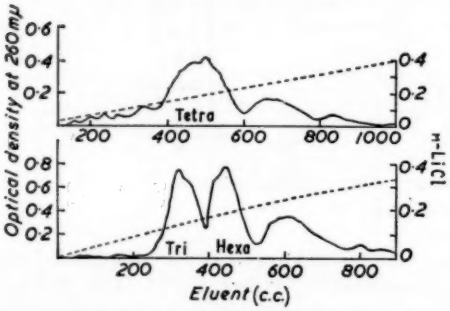


FIG. 7. *Chromatographic analysis of poly (AU) (upper curve) and poly (AAC) (lower curve) (after dialysis against water) on an "Ecteola" cellulose column* (12 × 1 cm.) *with gradient elution with aqueous lithium chloride. Flow rate* ~1 c.c./min. *Approx.* 7 mg. *of polymer.*

gave 5′-[2′(3′)-adenylyl]-, 5′-[2′(3′)-cytidylyl]-, 5′-[2′(3′)-guanylyl]-, and 5′-[2′(3′)-uridylyl]-adenosine respectively, in high yield and, in a number of cases, as crystalline compounds.

While separation of the 5′-2′- and 5′-3′-isomers of A2′(3′)P5′A, G2′(3′)P5′A, C2′(3′)P5′A and A2′(3′)P5′U on Dowex 1 anion-exchange resin was achieved, no useful fractionation of C2′(3′)P5′U or of U2′(3′)P5′A occurred. A direct estimate of the proportion of 5′-3′-linkage in these products, and in C2′(3′)P5′A, was obtained, however, on samples removed from the crude reaction mixtures. After preliminary purification by paper chromatography the mixture of isomers was treated with ribonuclease, then separated into nucleoside, nucleotide, and dinucleoside phosphate by paper chromatography or paper electrophoresis. Appropriate strips were eluted with dilute alkali, and the solutions were incubated at 37° to obviate the hypochromic effect, and analysed spectrophotometrically. The original mixture in each case contained some 50% of 5′-3′-linked dinucleoside phosphate, the remainder being 5′-2′, this result being analogous to those obtained by ion-exchange chromatography.

Differences in electrophoretic mobility between isomeric dinucleoside phosphates suggest that the 5′-2′-compounds are more compact or "streamlined" than the 5′-3′-isomers, *i.e.*, that stronger interaction occurs between the bases to restrict rotation about the internucleotide linkage. The alternative, that the 5′-2′-compounds are stronger acids, does not seem reasonable in view of the ion-exchange (Dowex 1) characteristics of the isomers examined. From the order of elution, in each case the 5′-3′-derivative behaved as a stronger acid. That the interplanar interaction is stronger in the 5′-2′-compounds is further indicated by a comparison of the hyperchromic effects. In general, the 5′-2′-isomer has a greater hyperchromicity than the 5′-3′-derivative (Table 3) as well as a greater electrophoretic mobility. It is perhaps significant also, that 5′-(2′-adenylyl)uridine showed a hyperchromicity twice that of the isomeric 5′-(2′-uridylyl)adenosine, *i.e.*, the increase in

ultraviolet absorption on degradation of polynucleotides depends on the order as well as the nature of the bases.

For the synthesis of trinucleoside diphosphates advantage was taken of the greatly disparate reactivities of the primary and secondary hydroxyl groups of ribonucleosides and their derivatives. Treatment of 5′-[2′(3′)-uridylyl]adenosine with 5′-*O*-acetylguanosine-2′,3′ cyclic phosphate and diphenyl phosphorochloridate, followed by removal of the acetyl group, gave a good yield of G2′(3′)P5′U2′(3′)P5′A, purified by ion-exchange chromatography and isolated as the free acid. As expected, acylation of the free 2′- and 3′-hydroxyl group of adenosine did not occur, nor was there significant cleavage of the dinucleoside phosphate—in the conditions employed, 5′-[2′(3′)-guanylyl]adenosine would have been formed had any such cleavage occurred. In a similar fashion, G2′(3′)P5′A2(3′)P5′U, U2′(3′)P5′G2′(3′)P5′A, C2′(3′)P5′U2′(3′)P5′A, and C2′(3′)P5′A2′(3′)P5′U were prepared from the appropriate acetylated nucleoside-2′,3′ cyclic phosphate and dinucleoside phosphate.

Repetition of this process, using an excess of $N^6O^{5'}$-diacetylcytidine-2′,3′ cyclic phosphate on G2′(3′)P5′A2′(3′)P5′U gave C2′(3′)P5′G2′(3′)P5′A2′(3′)P5′U, isolated as the free acid. In like manner, C2′(3′)P5′G2′(3′)P5′U2′(3′)P5′A and C2′(3′)P5′U2′(3′)P5′G2′(3′)P5′A were synthesised in good yield from the respective trinucleoside diphosphates.

TABLE 3. *Ultraviolet spectra.*

	In 0·01N-HCl			In 0·01N-NaOH			
Compound *	$\lambda_{max.}$ (mμ)	$\lambda_{min.}$ (mμ)	280/260 mμ	$\lambda_{max.}$ (mμ)	$\lambda_{min.}$ (mμ)	280/260 mμ	Alkaline hyperchromicity (%)
U2′(3′)P5′A	258	230	0·25	259	233	0·20	4·2
U2′P5′A	258	230	0·24	259	231	0·19	5·2
U3′P5′A	—	—	—	—	—	—	3·2
A2′P5′U	258	230	0·31	260	234	0·27	11·1
A3′P5′U	259	230	0·28	260	231	0·22	4·1
A5′P5′U	258	230	0·30	260	234	0·24	—
C2′(3′)P5′U	269	236	1·0	265	246	0·65	8·3
C2′P5′U	270	236	1·0	265	246	0·64	7·9
C3′P5′U	—	—	—	—	—	—	8·7
C2′P5′C	278	241	1·85	270	251	0·90	10·8
C3′P5′C	—	—	—	—	—	—	7·4
G2′P5′A	257	229	0·42	259	232	0·37	5·0
G3′P5′A	257	229	0·40	259	230	0·37	3·3
A2′P5′A	257	231	0·23	258	229	0·22	18·4
A3′P5′A	257	230	0·25	258	229	0·20	13·3
C2′P5′A	264	234	0·72	261	228	0·40	9·7
C3′P5′A	264	234	0·77	261	229	0·44	10·2
A3′P5′C (natural)	265	234	0·76	261	230	0·44	7·6
UpGpA	257	230	0·39	259	232	0·36	6·8
GpApU	257	229	0·40	259	232	0·37	11·3
GpUpA	257	229	0·39	259	231	0·34	5·3
CpApU	263	233	0·64	261	232	0·42	12·5
CpUpA	263	233	0·62	261	229	0·38	7·5
CpUpGpA	261	232	0·63	260	232	0·45	7·7
CpGpApU	261	232	0·63	260	231	0·45	12·9
CpGpUpA	261	232	0·62	260	233	0·45	6·2
GpCpApU	260	231	0·63	261	232	0·47	12·3
GpCpUpA	260	231	0·63	260	231	0·45	6·6
ApUpGpC	260	232	0·63	261	232	0·47	8·6
Poly ACGU	262	232	0·68	262	228	0·54	12·1

An alternative approach to tetranucleoside triphosphates with a defined order of bases, using acylation of a dinucleoside phosphate with a dinucleotide, was also successful. Small-scale preliminary experiments on the acylation of 2′,3′-di-*O*-acetyluridine and 2′,3′-di-*O*-acetyladenosine with 5′-(3′-adenylyl)cytidine-3′ phosphate, 5′-(3′-guanylyl)-cytidine-3′ phosphate, and 5′-(3′-adenylyl)uridine-3′ phosphate (isolated from an enzymic hydrolysate of yeast ribonucleic acid) demonstrated the feasibility of the method for the partial synthesis of six trinucleoside diphosphates, ApCpA, ApCpU, GpCpA, GpCpU, ApUpA, and ApUpU.* Although this work was not further pursued, extension to

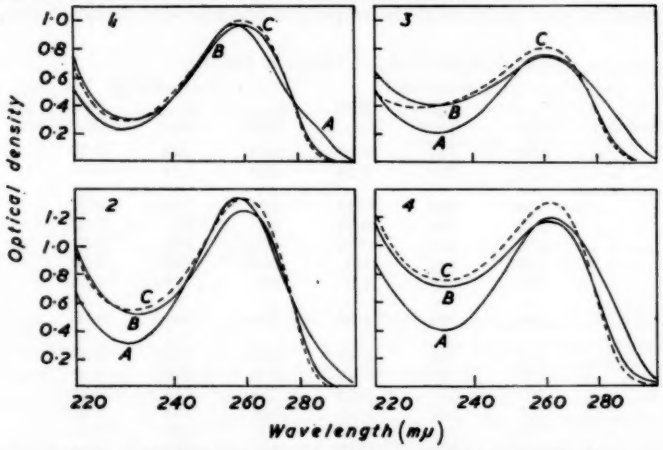
* p denotes the 2′P5′ or 3′P5′ linkage.

tetranucleoside triphosphates was equally successful. 5′-(3′-Guanylyl)cytidine-3′ phosphate was treated with ethyl chloroformate, to give a dinucleotide with a terminal 2′,3′-cyclic phosphate. This was then fully acetylated and the product treated with diphenyl phosphorochloridate and 5′-[2′(3′)-uridylyl]adenosine. Acetyl groups were removed with mild alkali, and the crude tetranucleoside triphosphate purified by ion-exchange chromatography to give a good yield of G2′(3′)P5′C2′(3′)P5′U2′(3′)P5′A, isolated as the free acid. Similar reactions of GpCp with ApU and of ApUp with GpC (acetylated at the cytosine N^6-position) yielded GpCpApU and ApUpGpC respectively.

Finally, copolymerisation of adenylic, cytidylic, guanylic, uridylic, and pseudouridylic acid with 5′-[2′(3′)-cytidylyl]adenosine yielded co-polymer ending with C2′(3′)P5′A, that is, a model of the " soluble RNA " concerned in protein biosynthesis.[8]

Degradation of the oligonucleotides was as expected. Treatment with alkali gave the respective mononucleotides and end nucleoside, while rattlesnake venom caused rapid breakdown to nucleosides, since a terminal 2′(or 3′)-phosphate was absent. The action of

FIG. 8. *Ultraviolet absorption spectra of* 1, G3′P5′A; 2, UpGpA; 3, CpUpGpA; 4, poly ACGU; *A, in* 0·01N-HCl; *B, in* 0·1N-NaOH; *C, alkaline hydrolysis products in* 0·1N-NaOH.



ribonuclease provided a final check on the structures of the synthetic compounds, the nature of the products being in accord with the specificity of this enzyme.[9] Thus, of the dinucleoside phosphates, only the pyrimidine nucleoside-3′P5′-purine(or -pyrimidine) nucleoside derivatives were degraded to 3′-phosphate and nucleoside, the others being unchanged; of the trinucleoside phosphates GpApU was undegraded, the others giving a range of products including unchanged material (2′P5′ linkage), dinucleotide, dinucleoside phosphate, nucleotide, and nucleoside, depending on the nature of the linkages and order of the bases. The tetranucleoside triphosphates also gave different products depending on the substrate; *e.g.*, CpGpApU gave C2′P5′GpApU, GpApU, and C3′P, while six products including adenosine and cytidine-3′ phosphate were obtained from CpGpUpA.

Ultraviolet absorption spectra illustrating the build up of a typical polynucleotide are shown in Fig. 8; Table 3 lists some optical properties of the synthetic compounds. A comparison of the hyperchromicities and other properties of the compounds described here and elsewhere [1,10] confirms the view that the anomalous ultraviolet absorption of a polynucleotide is a function, not only of nucleotide composition and chain length, but also of the order of bases, *i.e.*, it is a property of the entire molecule; that specious generalisations

[8] Hoagland, Stephenson, Scott, Hecht, and Zamecnik, *J. Biol. Chem.*, 1958, **231**, 241.
[9] Brown and Todd, in " The Nucleic Acids," ed. Chargaff and Davidson, Academic Press, New York, 1955, Vol. I, p. 409.
[10] Michelson, *Acta Biochem. Polon.*, 1959, **6**, 335.

concerning the effect of purines or pyrimidines are incorrect; that the effect is probably due to interaction between the purine and/or pyrimidine bases; and that because of this interaction there is restricted rotation about the internucleotide linkage even at the dinucleotide level. Any process which increases this interaction (*e.g.*, contraction of the macromolecule, metal chelation between rings) will increase the hypochromic effect, while a further diminution in absorption is caused by hydrogen-bonding between purine and pyrimidine rings of different chains or separate parts of the same chain.

Because of this restricted rotation,* oligonucleotides could act as templates (cf. the interaction of polyguanylic and polycytidylic acids of low molecular weight), a factor of possible significance for the chemical origin of life. Since these small polynucleotides give precipitates with protamine and bind planar basic dyes, it is possible that protection by small peptides would occur at relatively short chain lengths, giving rise to a process of natural selection at the molecular level and evolution from primitive oligonucleotide–peptides, to the present-day nucleoproteins. Some biological properties of proteins and nucleic acids are not entirely dependent on extremely high molecular weight.

Experimental

Polypseudouridylic Acid.—Mono(tri-n-octylammonium) pseudouridine-2′(3′) phosphate (from 50 mg. of the calcium salt) in dioxan (0·5 c.c.) was treated with diphenyl phosphorochloridate (0·08 c.c.) and tri-n-butylamine (0·17 c.c.), and the clear solution kept at room temperature for 3 hr. under anhydrous conditions. The polypseudouridylic acid was isolated as the ***calcium salt*** (30 mg.) in the usual manner (Found, in material dried at 110°/10^{-3} mm.: N, 8·4; P, 9·6. $[C_9H_{10}O_8N_2PCa_{\frac{1}{2}}]_x$ requires N, 8·6; P, 9·5%).

"Stable" Polycytidylic Acid.—Diphenyl phosphorochloridate (4·6 c.c.) and tri-n-butylamine (8·0 c.c.) were added to a solution of tri-n-butylammonium cytidine-2′,3′ cyclic phosphate (from 2·75 g. of cytidylic acid) in dimethylformamide (10 c.c.) and dioxan (15 c.c.), and the mixture was kept at room temperature for 24 hr. Solvent was removed and the polymer precipitated by ether (200 c.c.). The crude material was dissolved in aqueous ethanol, the pH adjusted to 3·0 by 2N-hydrochloric acid, and the solution kept at room temperature for 36 hr. Excess of ethanol and hydrochloric acid were then added and the precipitated polymer was centrifuged off, washed with ethanol, then ether, and dried (1·35 g.) (Found, in material dried at 110°/10^{-3} mm.: P, 10·5%).

Polycytidylic Acid.—Ethyl chloroformate (1·0 c.c.) was added to cytidine-2′(3′) phosphate (1·615 g.) and tri-n-butylamine (3·6 c.c.) in water (15 c.c.). The mixture was shaken vigorously for 5 min., then solvent was removed under reduced pressure and the residue dried by repeated evaporation with dioxan. The tri-n-butylammonium cytidine-2′,3′ cyclic phosphate was dissolved in dimethylformamide (15 c.c.) and dioxan (15 c.c.), redistilled acetic anhydride (0·5 c.c., 1·1 mol.) was added, followed by tri-n-butylamine (2·25 c.c.), and the solution kept at room temperature for 24 hr. Solvent was removed under reduced pressure, ether (75 c.c.) added to the residue with shaking, and the precipitated tri-n-butylammonium N^6-acetylcytidine-2′,3′ cyclic phosphate dried and dissolved in dimethylformamide (1·5 c.c.) and dioxan (10 c.c.). To this solution were added diphenyl phosphorochloridate (1·5 c.c.) and tri-n-butylamine (3·0 c.c.), and the mixture was kept at room temperature for 6 hr., then at 0° overnight. Solvent was removed under reduced pressure, ether (75 c.c.) added to the residue, and the precipitated polymer dissolved in water (45 c.c.). Ammonia was added to pH 9·6 and the solution kept at 37° for 18 hr. The solution was then concentrated to small volume, and ethanol and hydrochloric acid were added to precipitate the ***polycytidylic acid*** (1·46 g.) (Found, in material dried at 110°/10^{-3} mm.: N, 13·4; P, 9·9. $[C_9H_{12}O_7N_3P]_x$ requires N, 13·8; P, 10·2%).

No significant change in the spectrophotometrically determined (at 290 mμ), apparent pK_α (4·3) was observed on polymerisation of cytidylic acid.

Polycytidylic Acids of Low Molecular Weight.—A solution of tri-n-butylammonium N^4-acetylcytidine-2′,3′ cyclic phosphate [from 320 mg. of cytidine-2′(3′) phosphate] in dimethylformamide (1 c.c.) and dioxan (8 c.c.) was treated with diphenyl phosphorochloridate (0·3 c.c.) and tri-n-butylamine (0·6 c.c.) at room temperature for 3 hr., and the product isolated as previously described [1] (220 mg.).

* Confirmatory evidence is provided by the photochemical behaviour of the synthetic polyuridylic acids (D. Shugar, personal communication) and by the ultraviolet absorption changes induced in the synthetic polyadenylic acids by interaction with mercuric chloride (C. A. Dekker, personal communication).

Poly ACGU.—Equimolar quantities of the tri-n-butylammonium salts of adenosine-2′,3′ cyclic phosphate, guanosine-2′,3′ cyclic phosphate, uridine-2′,3′ cyclic phosphate, and N^6-acetylcytidine-2′,3′ cyclic phosphate [from 323 mg. of cytidine-2′(3′) phosphate] were dissolved in dimethylformamide (2 c.c.) and dioxan (10 c.c.) and treated with diphenyl phosphorochloridate (1·2 c.c.) and tri-n-butylamine (2·4 c.c.) in the usual way. The final product was dissolved in water, ammonia was added to pH 9·6, and the solution was kept at 37° for 18 hr. to remove acetyl groups. The copolymer was isolated in the normal manner, as the free acid (1·17 g.).

Countercurrent Distribution (By Dr. K. S. KIRBY).—A two-phase system of Cellosolve–2-methoxyethanol–2-ethoxyethanol (2 : 8 : 3) (16 parts by volume), water (25 parts) and phosphate buffer (25 parts) was used with 96 transfers in each case. The phosphate buffer used was aqueous dipotassium hydrogen phosphate (*d* 1·32)–33% (v/v) phosphoric acid (50 : 3). With this system, countercurrent distribution of adenosine-3′ phosphate, cytidine-3′ phosphate, guanosine-3′ phosphate, uridine-3′ phosphate, and 5-(3′-adenylyl)cytidine-3′ phosphate (A3′P5′C3′P) gave curves in good agreement with those determined theoretically, with peaks at tube numbers 51, 39, 42, 42, and 52 respectively.

Paper Chromatography.—Ascending chromatograms on Whatman No. 1 paper were used with solvent systems: *A*, ethanol–M-ammonium acetate (5 : 2); *B*, t-pentyl alcohol–formic acid–water (3 : 2 : 1), results being as tabulated.

	R_F			R_F	
	A	*B*		*A*	*B*
Cytidine-2′(3′) phosphate	0·16	0·41	CpCpC	0·12	01·3
CpCp	0·04	0·23	CpCpCpC	0·06	0·06
CpCpCp	0·01	0·12	Polycytidylic acid	0·0	0·0—0·1
CpCpCpCp	0·0	0·03	Pseudouridine-2′(3′) phosphate	0·13	0·32
CpC	0·32	0·29	Polypseudouridylic acid	0·0	0·0

Paper Electrophoresis.—Movements towards the anode on Whatman No. 1 paper at 10 v/cm. for 2 hr. in (I) M/50-Na_2HPO_4, and (II) M/50-KH_2PO_4, respectively were: pseudouridylic acid 10·3, 7·9; polypseudouridylic acid 11·4, 10·1; cytidylic acid 10·5, 8·3; polycytidylic acid 11·3, 9·3; " stable " polycytidylic acid 7·7—10·5, 3·3—7·6; polyguanylic acid 9·0; mixture of polyguanylic and polycytidylic acid 10·5 cm.

General Method for the Preparation of Nucleoside-2′,3′ Cyclic Phosphates.—To a solution of the nucleoside-2′(3′) phosphate (1 mmole) in water (3 c.c.) was added tri-n-butylamine (0·72 c.c., 5 mmoles), followed by ethyl chloroformate (0·19 c.c., 2 mmoles), and the mixture was shaken vigorously for 5—10 min. Solvent was then removed under reduced pressure and the residue dried by evaporation with ethanol. The nucleotide was isolated by precipitation with ether or as the barium salt on addition of a methanolic solution of barium bromide. Identity with authentic specimens was established by paper chromatography, paper electrophoresis, and behaviour towards acid, alkali, and ribonuclease. For biochemical purposes the tri-n-butylamine in the above preparation may be replaced by triethylamine or sodium hydrogen carbonate (Dr. W. F. Hemmens). Replacement of the nucleotide by β-glycerophosphate or 2-hydroxyethyl phosphate gave quantitative yields of the corresponding cyclic phosphates.

Isolation of Natural Oligonucleotides from Yeast Ribonucleic Acid.—Yeast ribonucleic acid (50 g.) was exhaustively treated with ribonuclease and the mixture then dialysed against water. The dialysate, containing largely mononucleotides, dinucleotides, and trinucleotides, was fractionated on Dowex 1 × 2 (chloride form) as described by Volkin and Cohn.[6] Appropriate fractions were combined and refractionated on smaller columns with the eluting agents as shown:

A3′P5′A3′P5′C3′P	0·01N-hydrochloric acid, 0·0125M-lithium chloride
G3′P5′C3′P	0·01N-hydrochloric acid, 0·0125M-lithium chloride
A3′P5′U3′P	0·01N-hydrochloric acid, 0·025M-lithium chloride

Each compound was isolated as the free acid by precipitation with ethanol and hydrochloric acid, identified by the usual methods, and further characterised by treatment with prostate monoesterase to remove the terminal phosphate. Purified monoesterase (4 mg.) was added to a solution of the substrate (400 mg.) in citrate buffer (40 c.c.) at pH 5·3 and the mixture incubated at 37° for 9 hr. The solution was then diluted to 100 c.c., adjusted to pH 9, and run on to a column of Dowex 1 × 2 (formate form). Elution with dilute formic acid followed by evaporation of the appropriate fractions to dryness under reduced pressure gave the free *acids*, which were precipitated from concentrated aqueous solution by the addition of ethanol. The normality of formic acid used for removal of the various compounds from the Dowex 1 × 2 resin was:

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A3′P5′C (0·015); G3′P5′C (0·04); A3′P5′U (0·05); A3′P5′A3′P5′C (0·075). The G3′P5′C crystallised from water as clusters of long thin needles.

Analyses are tabulated.

Compound	Found N (%)	Found P (%)	Formula	Required N (%)	Required P (%)
A3′P5′A3′P5′C3′P	18·8	9·4	$C_{29}H_{36}O_{20}N_{13}P_3$	18·6	9·5
A3′P5′A3′P5′C	20·0	7·0	$C_{29}H_{37}O_{17}N_{13}P_2$	20·2	6·9
G3′P5′C3′P	16·4	9·3	$C_{19}H_{26}O_{15}N_6P_2$	16·8	9·3
G3′P5′C	18·9	5·3	$C_{19}H_{25}O_{12}N_6P$	19·0	5·3
A3′P5′U3′P	15·2	9·4	$C_{19}H_{25}O_{15}N_7P_2$	15·0	9·5
A3′P5′U	16·9	5·3	$C_{19}H_{24}O_{12}N_7P$	17·1	5·4
A3′P5′C	19·6	5·4	$C_{19}H_{25}O_{11}N_6P$	19·6	5·4

Apparent pK_a's were spectrophotometrically determined at the wavelengths indicated: G3′P5′C3′P, 4·4 (280 mμ), 9·65 (265 mμ); G3′P5′C, 4·15 (280 mμ), 9·6 (265 mμ); A3′P5′C3′P, 4·25 (290 mμ); A3′P5′C, 4·15 (290 mμ).

5′-(3′-*Adenylyl*)*adenosine* (*Natural*).—Stepwise degradation of A3′P5′A3′P5′C3′P by prostate monoesterase and periodate oxidation [11] gave diadenylic acid. The terminal phosphate was removed and the product purified by ion-exchange chromatography on Dowex 1 (formate form) with 0·025N-formic acid as eluting agent. 5′-(3′-*Adenylyl*)*adenosine* crystallised from water as rosettes of needles, softening at 184—186°, decomp. 204° (Found, in material dried at 100°/1 mm. for 24 hr.: N, 23·1; P, 5·2. $C_{20}H_{25}O_{10}N_{10}P$ requires N, 23·5; P, 5·2%).

Poly (*AU*).—Ethyl chloroformate (0·08 c.c.) was shaken with tri-n-butylamine (0·30 c.c.) and 5′-(3′-adenylyl)uridine-3′ phosphate (135 mg., 0·2 mmole) in water (1·5 c.c.), for 10 min. Solvent was then removed under reduced pressure, and the residue dried by evaporation with dimethylformamide and kept overnight at room temperature at 10^{-2} mm. over phosphoric oxide. A solution of this tri-n-butylammonium adenylyluridine cyclic phosphate in dimethylformamide (1 c.c.) and dioxan (0·5 c.c.) was treated with tri-n-butylamine (0·2 c.c.) and diphenyl phosphorochloridate (0·1 c.c.) at room temperature for 6 hr. Solvent was removed under reduced pressure, and the polymer precipitated with ether and worked up as a calcium salt in the usual way (130 mg.). Paper chromatography showed unchanged dimer, tetramer, and higher oligonucleotides and traces of monomer and trimer.

Poly (*AC*) *and Poly* (*GC*).—The dinucleotide (0·2 mmole) was first treated with ethyl chloroformate as described above. To a solution of the anhydrous product in dimethylformamide (3 c.c.) and dioxan (1 c.c.) were then added tri-n-butylamine (0·1 c.c.) and acetic anhydride (0·022 c.c., 0·22 mmole), and the solution was kept at room temperature for 36 hr. Solvent was removed under reduced pressure and the residue shaken with cyclohexane (5 c.c.), then with ether (5 c.c.). The precipitated material was dried, then dissolved in dimethylformamide (1 c.c.) and dioxan (0·5 c.c.) and treated with diphenyl phosphorochloridate (0·1 c.c.) and tri-n-butylamine (0·2 c.c.) at room temperature for 6 hr. Ether (10 c.c.) was added, and an aqueous solution of the precipitated polymer was kept at pH 9·8 at 37° for 12 hr. Precipitation with ethanol and hydrochloric acid gave the crude polymer mixture (100 mg.).

Poly (*AAC*).—The phosphate A3′P5′A3′P5′C3′P (110 mg., 0·1 mmole) was treated successively with ethyl chloroformate (0·05 c.c.), acetic anhydride (0·015 c.c.), and diphenyl phosphorochloridate (0·085 c.c.) as described for the polymerisation of 5′-(3′-adenylyl)cytidine-3′ phosphate. The *product* was isolated in the usual way (99 mg.) (Found, in material dried at 100°/1 mm. for 24 hr.: N, 18·5; P, 9·3. $[C_{29}H_{36}O_{19}N_{13}P_3]_x$ requires N, 18·9; P, 9·7%).

Paper Chromatography.—Ascending chromatograms on Whatman No. 1 paper were used with solvent systems: *A*, ethanol–M-ammonium acetate (5 : 2); *B*, t-pentyl alcohol–formic acid–water (3 : 2 : 1). Results are tabulated as R_F's.

	A	*B*		*A*	*B*
A3′P5′A3′P5′C3′P	0·02	0·11	A3′P5′C3′P	0·06	0·22
A3′P5′A3′P5′C	0·08	0·14	A3′P5′C	0·25	0·27
A3′P5′A3′P	0·04	0·22	G3′P5′C3′P	0·04	0·16
A3′P5′A	0·23	0·30	G3′P5′C	0·20	0·22
A3′P	0·14	0·44	A3′P5′U3′P	0·06	0·24
Adenosine	0·60	0·64	A3′P5′U	0·31	0·29
N^6-Acetyl (ApApC2′,3′p)	—	0·19	N^6-Acetyl(GpC2′,3′P)	—	0·26
N^6-Acetyl(ApC2′,3′p)	—	0·32			

[11] Whitfeld and Markham, *Nature*, 1953, **171**, 1151; Brown, Fried, and Todd, *J.*, 1955, 2206.

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Paper Electrophoresis.—Movement (cm.) towards the anode is tabulated, for Whatman No. 1 paper, with (I) M/50-Na_2HPO_4 and (II) M/50-KH_2PO_4, both at 10 v/cm. for 2 hr.

	I	II		I	II
A3′P5′A3′P5′C3′P	10·1	8·3	A3′P5′C3′P	9·8	8·1
A3′P5′A3′P5′C	6·4	6·2	A3′P5′C	4·8	4·7
A3′P5′A3′P	9·9	8·1	G3′P5′C3′P	10·1	8·1
A3′P5′A	4·3	3·7	G3′P5′C	4·8	4·0
A3′P	9·3	6·9	A3′P5′U3′P	10·0	8·1
Poly (AAC)	11·2	9·2	A3′P5′U	5·2	4·9
Poly (AC)	10·5	8·9	Poly (AU)	10·8	9·3
Poly (GC)	10·6	8·5			

Acetylated Nucleoside-2′,3′ Cyclic Phosphates.—Ethyl chloroformate (0·2 c.c.) was shaken with a solution of the nucleotide (1 mmole) and tri-n-butylamine (0·75 c.c.) in water (3 c.c.) for 10 min., to prepare the 2′,3′-cyclic phosphate. Solvent was removed under reduced pressure, and the anhydrous residue dissolved in dimethylformamide (3 c.c.) and dioxan (3 c.c.). Acetic anhydride (0·5 c.c.) and tri-n-butylamine (1·45 c.c.) were added and the solution was kept at room temperature for 48 hr.; paper chromatography then showed that acetylation was complete. Solvent was removed and anhydrous ether (50 c.c.) added to the residue. The precipitated tri-n-butylammonium 5′-*O*-acetylnucleoside-2′,3′ cyclic phosphate ($N^6O^{5'}$-diacetyl in the case of cytidylic acid) was washed with ether by decantation and dried. Paper chromatography showed that the product was homogeneous with respect to ultraviolet-absorbing material. Yields were quantitative. Absorption maxima were as tabulated.

	In 0·04N-HCl			In water (pH 7)			In 0·04N-NaOH		
2′,3′-Cyclic phosphates	$\lambda_{max.}$ (mμ)	$\lambda_{min.}$ (mμ)	280/260 mμ	$\lambda_{max.}$ (mμ)	$\lambda_{min.}$ (mμ)	280/260 mμ	$\lambda_{max.}$ (mμ)	$\lambda_{min.}$ (mμ)	280/260 mμ
N^6-Acetylcytidine	244, 302	225, 270	0·92	246, 295	225, 271	0·60	298	237	1·51
$N^6O^{5'}$-Diacetylcytidine	244, 302	225, 270	0·90	246, 295	225, 271	0·60	298	237	1·45
5′-*O*-Acetyladenosine	256	230	0·31	258	228	0·16	258	230	0·22
5′-*O*-Acetylguanosine	255	227	0·71	252	222	0·71	261	231	0·63
5′-*O*-Acetyluridine	258	228	0·22	257	228	0·21	259	242	0·30

Dinucleoside(-3′,-5′) Phosphates.—A solution of tri-n-butylammonium 5′-*O*-acetyl-nucleoside-2′,3′ cyclic phosphate [from 1 mmole of the 2′(or 3′) phosphate] in dioxan (4 c.c.) [in the case of guanylic acid a mixture of dimethylformamide (2 c.c.) and dioxan (2 c.c.) was used] was added to the anhydrous 2′,3′-di-*O*-acetyl-nucleoside (1 mmole). Diphenyl phosphorochloridate (0·3 c.c.) was then added, followed by tri-n-butylamine (0·6 c.c.), and the clear solution was kept at room temperature under anhydrous conditions for 18 hr. Solvent was removed under reduced pressure and ether (50 c.c.) added to the residue with shaking. The precipitated material was dried, then dissolved in water (10 c.c.), ammonia being added to pH 9·8, and the solution was extracted twice with ether, the extracts being discarded. The aqueous solution was kept at pH 9·8 at 37° for 48 hr., then diluted and run on a column (12 × 1·2 cm.) of Dowex 1 (formate) resin which was then washed with water; the dinucleoside phosphate was eluted with dilute formic acid. Appropriate fractions were combined and evaporated to dryness under reduced pressure. The residue was dissolved in water, then ethanol or acetone was added to give the dinucleoside phosphate as the free acid, which in a number of cases readily crystallised from water or aqueous ethanol.

Yields of dinucleoside phosphate isolated in pure solid form were: ApA, 53%; CpA, 60%; GpA, 40%; UpA, 58%; ApU, 60%; CpU, 65%; from equimolar proportions of phosphate and diacetyl-nucleoside. These yields could be improved relative to the nucleoside by using an excess of the acetylated nucleoside cyclic phosphate.

The apparent pK_a of 5-(2′-cytidylyl)adenosine was 4·35, and of 5′-(3′-cytidylyl)adenosine 4·25, both determined spectrophotometrically at 290 mμ.

Trinucleoside Diphosphates.—A solution of the tri-n-butylammonium dinucleoside phosphate (0·5 mmole) and tri-n-butylammonium 5′-*O*-acetyl-nucleoside-2′,3′ cyclic phosphate [or in the case of cytidylic acid the $N^6O^{5'}$-diacetyl derivative] (1 mmole) in dimethylformamide (2 c.c.) and dioxan (1·0 c.c.) was treated with diphenyl phosphorochloridate (0·45 c.c.) and tri-n-butylamine (0·90 c.c.) at room temperature for 12 hr. Solvent was removed under reduced pressure, ether (75 c.c.) added to the residue, and the precipitated material dissolved in water (10 c.c.). Ammonia was added to pH 9·8, amines were removed by extraction twice with ether,

and the aqueous solution was kept at pH 9·8 at 37° for 47 hr. The diluted solution, shown by paper chromatography to contain nucleotide, dinucleoside phosphate, and trinucleoside diphosphate, was run on a column (12 × 1·2 cm.) of Dowex 1 × 2 resin (chloride form), and the column was eluted with 0·01N-hydrochloric acid, then with lithium chloride in 0·01N-hydrochloric acid. Appropriate fractions were combined, neutralised with triethylamine, and concentrated to small volume under reduced pressure. Ethanol and dilute hydrochloric acid were then added, to precipitate the trinucleoside diphosphate as the free acid. The material was collected by centrifugation, washed with ethanol, then ether, and dried. Yields ranged from 20 to 35% or, after allowance for recovered material, 30—60% based on the dinucleoside phosphate used.

Tetranucleoside Triphosphates from Trinucleoside Diphosphates.—A solution of tri-n-butylammonium trinucleoside diphosphate (0·03 mmole) and tri-n-butylammonium $N^6O^{5'}$-diacetyl-nucleoside-2′,3′ cyclic phosphate (0·12 mmole) in dimethylformamide (0·2 c.c.) and dioxan (0·4 c.c.) was treated with diphenyl phosphorochloridate (0·06 c.c.) and tri-n-butylamine (0·12 c.c.) at room temperature for 4 hr., then worked up in the usual way. Acetyl groups were removed at pH 9·8 and the crude products purified by ion-exchange chromatography on Dowex 1 resin (chloride form). Appropriate fractions were combined, neutralised with triethylamine, and evaporated to small volume under reduced pressure. Addition of ethanol and dilute hydrochloric acid precipitated the tetranucleoside triphosphates as fine white powders which were collected by centrifugation, washed with ethanol, then ether, and dried. The yields of isolated material were ~40%. As unchanged material was recovered, the yield based on the trinucleoside diphosphate used was 75—80%.

Tetranucleoside Triphosphates from Dinucleoside Phosphates.—Ethyl chloroformate (0·08 c.c.) was shaken with the dinucleotide (0·2 mmole) and tri-n-butylamine (0·3 c.c.) in water (1·5 c.c.) for 10 min. Solvent was removed and the anhydrous residue dissolved in dimethylformamide (3 c.c.) and dioxan (1 c.c.). Acetic anhydride (0·15 c.c.) and tri-n-butylamine (0·45 c.c.) were added and the solution was kept at room temperature under anhydrous conditions for 48 hr. Solvent was removed under reduced pressure and ether (10 c.c.) added to precipitate the acetylated dinucleotide containing a terminal cyclic phosphate. This product was dried, dissolved in dimethylformamide (1 c.c.) and dioxan (0·5 c.c.), and added to the tri-n-butylammonium dinucleoside phosphate (0·1 mmole). To the clear solution were added diphenyl phosphorochloridate (0·15 c.c.) and tri-n-butylamine (0·3 c.c.), and the mixture was kept at room temperature for 6 hr., then worked up as previously described. Acetyl groups were removed at pH 9·8 at 37° (48 hr.) and the crude tetranucleoside triphosphate purified by ion-exchange chromatography.

In the case of dinucleoside phosphates containing cytosine it was necessary to protect the 6-amino-group by partial acetylation in aqueous dimethylformamide, before reaction of the dinucleotide and diphenyl phosphorochloridate.

Yields of isolated material ranged from 25 to 50%; allowance for unchanged materials recovered from the ion-exchange fractionation increased the yields to 50—75% based on dinucleoside phosphate used.

Ion-exchange Chromatography.—For purification and separation of the various nucleotide derivatives ion-exchange chromatography on columns of Dowex 1 × 2 resin, both formate and chloride form, was used, with the eluting agents tabulated for the respective compounds.

	Normality of $H{\cdot}CO_2H$ used to elute compound from resin (formate form)		Molarity of LiCl in 0·01N-HCl used to elute compound after washing with 0·01N-HCl
ApA	0·025	UpGpA	0·0375
CpA	0·01	GpUpA	
GpA	0·09	GpApU	
UpA	0·05	CpUpGpA	0·025
ApU	0·05	CpGpUpA	
CpU	0·025	CpGpApU	0·0375
CpApU	0·15	ApUpGpC	
CpUpA	0·15	GpCpApU	0·05
		GpCpUpA	

Separation of U2′(3′)P5′A from A3′P5′U was obtained on Dowex 1 resin (formate form), the peaks being at fraction numbers 44 and 60 respectively.

Where necessary the oligonucleotide was further purified by paper chromatography before spectroscopic examination; some degradation appeared to occur during the working up of

the higher polymers, possibly because of the high salt concentration on evaporation to small volume and the acidic conditions used for precipitation.

Co-polymer Terminating with 5′-[2′(3′)-Cytidylyl]adenosine.—Adenosine-2′(3′) phosphate (116 mg.), guanosine-2′(3′) phosphate (121 mg.), uridine-2′(3′) phosphate (88 mg.), and pseudouridine-2′(3′) phosphate (20 mg.) were added to water (3 c.c.) and tri-n-butylamine (0·75 c.c.) and treated with ethyl chloroformate (0·2 c.c.) at room temperature for 10 min. Solvent was removed, the anhydrous residue dissolved in dimethylformamide (1·5 c.c.) and dioxan (2 c.c.) and added to N^6-acetylcytidine-2′,3′ cyclic phosphate (from 108 mg. of cytidylic acid) and 5′-[N^6-acetyl-2′(3′)-cytidylyl]adenosine (from monoacetylation of 200 mg. of the dinucleoside phosphate with 0·04 c.c. of acetic anhydride). The mixture was treated with diphenyl phosphorochloridate (0·5 c.c.) and tri-n-butylamine (1 c.c.) at room temperature for 4 hr. and worked up in the normal way, acetyl groups being removed at pH 9·8. The crude polymer mixture was dialysed against 2M-sodium chloride and isolated as the free acid (120 mg.). Light absorption: in 0·01N-HCl, $\lambda_{max.}$ 264, mμ, $\lambda_{min.}$ 233 mμ, density ratio 280/260 mμ 0·76; in 0·1N-NaOH, $\lambda_{max.}$ 262 mμ, $\lambda_{min.}$ 233 mμ, density ratio 280/260 mμ 0·52. Alkaline hyperchromicity, 13·3%.

Degradation of Nucleotide Derivatives.—(a) *With ribonuclease.* Ribonuclease (0·05 c.c. of a solution containing 2 mg. of 5 times recrystallised ribonuclease per c.c.) was added to the substrate (1—1·5 mg.) in water (0·15 c.c.) and glycine buffer (0·05 c.c.; pH 7), and the mixture was incubated at 37° for 48 hr.

(b) *With rattlesnake* (Crotalus atrox) *venom.* Venom (0·05 c.c. of a solution containing 10 mg./c.c.) was added to the substrate (1—1·5 mg.) in water (0·15 c.c.) and glycine buffer (0·05 c.c.; pH 9), and the mixture was incubated at 37° for 48 hr.

(c) *With alkali.* The material (~1 mg.) was treated with 0·1N-sodium hydroxide at 37° for 48 hr.

Products were identified by paper chromatography in solvents A and B and in the propan-2-ol–hydrochloric acid solvent described by Wyatt.[12]

Paper Chromatography.—Ascending chromatograms on Whatman No. 1 paper were used with solvent systems; *A*, ethanol–M-ammonium acetate (5 : 2); *B*, t-pentyl alcohol–formic acid–water (3 : 2 : 1). Results are tabulated.

	A	*B*		*A*	*B*
A2′(3′)P	0·14	0·44	A2′P5′A	0·23	0·30
C2′(3′)P	0·16	0·41	A3′P5′A	0·24	0·30
G2′(3′)P	0·10	0·33	A3′P5′A (natural)	0·24	0·30
U2′(3′)P	0·21	0·43	C2′P5′A	0·27	0·29
ψU2′(3′)P	0·13	0·32	C3′P5′A	0·28	0·30
			A3′P5′C (natural)	0·25	0·27
U2′(3′)P5′A	0·33	0·30	A2′P5′U	0·30	0·29
C2′(3′)P5′U	0·33	0·28	A3′P5′U	0·31	0·29
G2′P5′A	0·20	0·26	A3′P5′U (natural)	0·31	0·29
G3′P5′A	0·20	0·24	A5′P5′U	0·26	0·24

In the following compounds p signifies a phosphate linkage from the 2′(or 3′)-hydroxyl of the nucleoside on the left to a 5′-hydroxyl of the nucleoside on the right.

UpGpA	0·10	0·12	CpUpGpA	0·03	0·06
GpApU	0·09	0·12	CpGpApU	0·03	0·07
GpUpA	0·08	0·12	CpGpUpA	0·03	0·06
CpApU	0·12	0·14	GpCpApU	0·03	0·07
CpUpA	0·13	0·14	GpCpUpA	0·03	0·06
			ApUpGpC	0·02	0·05

2′,3′-Cyclic phosphates

Adenosine	0·41	0·44
5′-*O*-Acetyladenosine	0·60	0·53
Cytidine	0·43	0·41
N^6-Acetylcytidine	0·54	0·50
$N^6O^{5'}$-Diacetylcytidine	0·68	0·58
Guanosine	0·37	0·33
5′-*O*-Acetylguanosine	0·53	0·46
Uridine	0·47	0·43
5′-*O*-Acetyluridine	0·62	0·56
5′-[N^6-Acetyl-2′(3′)-cytidylyl]adenosine	—	0·36

[12] Wyatt, *Biochem. J.*, 1951, **48**, 584.

Paper Electrophoresis.—Movement (cm.) towards the anode is tabulated, for Whatman No. 1 paper, with (I) M/50-Na_2HPO_4 (pH 8·9) and (II) M/50-KH_2PO_4 (pH 4·5), both at 10 v/cm. for 2 hr.

	I	II		I	II
A2′(3′)P	9·3	6·9	A2′P5′A	5·0	4·5
C2′(3′)P	10·5	8·2	A3′P5′A	4·3	3·7
G2′(3′)P	9·6	7·4	A3′P5′A (natural)	4·3	3·7
U2′(3′)P	11·1	8·8	C2′P5′A	5·4	4·7
ψU2′(3′)P	10·8	8·0	C3′P5′A	4·8	4·6
			A3′P5′C (natural)	4·8	4·7
U2′(3′)P5′A	5·7	5·0	A2′P5′U	5·3	6·0
C2′(3′)P5′U	6·5	5·9	A3′P5′U	5·2	4·9
G2′P5′A	5·5	5·0	A3′P5′U (natural)	5·2	4·9
G3′P5′A	5·0	4·3	A5′P5′U	5·6	5·7
UpGpA	6·9	7·6	CpUpGpA	8·7	7·9
GpApU	6·9	7·3	CpGpApU	8·9	8·5
GpUpA	6·5	6·8	CpGpUpA	8·5	6·9
CpApU	7·7	7·6	GpCpApU	8·7	8·0
CpUpA	7·2	7·3	GpCpUpA	8·3	7·6
			ApUpGpC	8·3	7·6

2′,3′-Cyclic phosphates	I	II
Adenosine	5·3	6·9
5′-*O*-Acetyladenosine	5·1	6·8
Cytidine	6·3	8·2
N^6-Acetylcytidine	6·1	8·1
$N^6O^{5'}$-Diacetylcytidine	5·6	7·3
Guanosine	5·7	7·4
5′-*O*-Acetylguanosine	5·3	7·4
Uridine	6·8	8·8
5′-*O*-Acetyluridine	6·5	8·0

Analyses.—The free *acids* were dried at 110°/10^{-3} mm. for 24 hr. (see Table).

	Found			Required	
Compound	N (%)	P (%)		N (%)	P (%)
U2′(3′)P5′A	16·9	5·3	$C_{19}H_{24}O_{12}N_7P$	17·1	5·4
A2′P5′U	17·2	5·4	$C_{19}H_{24}O_{12}N_7P$	17·1	5·4
A3′P5′U	16·8	5·6	$C_{19}H_{24}O_{12}N_7P$	17·1	5·4
C2′(3′)P5′U	12·5	5·7	$C_{19}H_{24}O_{13}N_5P$	12·7	5·6
G2′P5′A	23·0	4·9	$C_{20}H_{25}O_{11}N_{10}P$	22·9	5·1
G3′P5′A	22·7	5·0	$C_{20}H_{25}O_{11}N_{10}P$	22·9	5·1
A2′P5′A	23·2	5·2	$C_{20}H_{25}O_{10}N_{10}P$	23·5	5·2
A3′P5′A	23·3	5·2	$C_{20}H_{25}O_{10}N_{10}P$	23·5	5·2
C2′P5′A	19·7	5·4	$C_{19}H_{25}O_{11}N_8P$	19·6	5·4
C3′P5′A	19·4	5·6	$C_{19}H_{25}O_{11}N_8P$	19·6	5·4
UpGpA	18·0	6·8	$C_{29}H_{36}O_{19}N_{12}P_2$	18·3	6·8
GpApU	—	7·0	$C_{29}H_{36}O_{19}N_{12}P_2$	18·3	6·8
GpUpA	—	7·1	$C_{29}H_{36}O_{19}N_{12}P_2$	18·3	6·8
CpApU	—	7·3	$C_{28}H_{36}O_{19}N_{10}P_2$	15·9	7·1
CpUpA	—	7·1	$C_{28}H_{36}O_{19}N_{10}P_2$	15·9	7·1
CpUpGpA	—	7·7	$C_{38}H_{48}O_{26}N_{15}P_3$	17·2	7·6
CpGpApU	—	7·4	$C_{38}H_{48}O_{26}N_{15}P_3$	17·2	7·6
CpGpUpA	—	7·8	$C_{38}H_{48}O_{26}N_{15}P_3$	17·2	7·6
GpCpApU	—	7·5	$C_{38}H_{48}O_{26}N_{15}P_3$	17·2	7·6
GpCpUpA	—	7·6	$C_{38}H_{48}O_{26}N_{15}P_3$	17·2	7·6
ApUpGpC	—	7·7	$C_{38}H_{48}O_{26}N_{15}P_3$	17·2	7·6

When recrystallised from water, C2′P5′A and G2′P5′A formed long thin needles; A2′P5′A and A2′P5′U formed monoclinic prisms; and A3′P5′A formed rosettes of small needles. As means of characterisation m. p. were unsatisfactory, all of the compounds softening and darkening at 190—200° and decomposing at 200—220°; nor were mixed m. p.s valid for identification.

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Arthur Guinness Son & Co. (Dublin) Ltd.,
Dublin, Ireland.

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746. *Infrared Absorption of Heteroaromatic and Benzenoid Six-membered, Monocyclic Nuclei. Part IX.*[1] ortho-*Disubstituted Benzenes.*

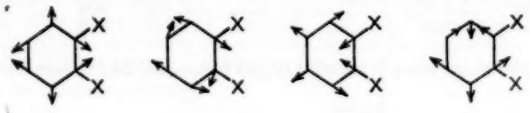
By A. R. Katritzky and R. A. Jones.

Absorption due to the *ortho*-disubstituted benzene ring for 45 compounds is recorded and discussed.

Following our work on *para*-[2] and *meta*-disubstituted benzenes,[1] we now report on 45 *ortho*-compounds. The object of the work, the conditions of measurement, the regions of the spectrum investigated, and the arrangement of the Table have been discussed,[2] as has the classification of substituents, into donor (*d*), acceptor (*a*), halogen (*x*), and weak (*w*), on the basis of their electronic effects.[2]

Randle and Whiffen [3] treated statistically the spectra of many *ortho*-disubstituted benzenes and listed arithmetic means and standard deviations for eleven bands in the 1600—800 cm.$^{-1}$ region (see below), which they assigned on the basis of earlier work on both Raman and infrared spectra (the assignments in this paper are as in ref. 3). However, they obtained data from many sources, measured under varying conditions, and were unable to give any indication of quantitative intensities or to relate the intensity or position of bands to the nature of the substituents.

Ring-stretching Frequencies at ca. 1600—1400 *cm.*$^{-1}$.—Four bands occur in this region corresponding to the vibration modes (I—IV). The first band (I) (col. 1) occurs at 1576—



(I) (II) (III) (IV)

1570 cm.$^{-1}$ when the substituents are two halogen atoms, at 1602—1591 [1595 ± 5] cm.$^{-1}$ where one of the substituents is a halogen atom, and at 1624—1591 [1607 ± 9] cm.$^{-1}$ otherwise.*

da	*dd, dx, xa*	*dw, wa, aa*	*xx, xw, ww*
(140—330)	(60—150)	(15—65)	(10—25)
[210 ± 60]	[90 ± 25]	[40 ± 15]	[20 ± 7]

The intensity varies with the substituents in a manner intermediate between that shown by *para*-substituted benzenes (where the intensity varies as the difference in the electronic effects of the substituents) and that shown by *meta*-substituted benzenes (where the intensity varies as the sum of the electronic effects of the substituents).[1,2]

Many of the compounds show a second band (II) (col. 2) at 1593—1578 [1587 ± 5] cm.$^{-1}$ for *da* compounds (except No. 21) and at 1584—1571 [1577 ± 4] cm.$^{-1}$ otherwise. The intensity is (90—300) [(140 ± 65)] for *da* compounds, (20—85) [(40 ± 20)] for *aa*, *xw*, *xa*, and *wa* compounds; for other compounds the band is found only as a shoulder or not at all.

A third band (III) (col. 3) occurs at 1514—1452 cm.$^{-1}$ (20—460); both position and

dd		*dw*		*dx, ww, da, wa, aa*		*xa, xw*		*xx*
1514—1505	>	1503—1495	>	1498—1458	>	1478—1466	>	1460—1452
[1508 ± 4]		[1500 ± 4]		[1487 ± 5]		[1470 ± 5]		[1455 ± 4]

* Parentheses indicate apparent molecular extinction coefficients, and square brackets arithmetic means and standard deviations. The intensities of shoulders and superimposed bands and the position of shoulders are not treated statistically.

[1] Katritzky and Simmons, *J.*, 1959, 2058.
[2] *Idem*, *J.*, 1959, 2051.
[3] Randle and Whiffen, Paper no. 12, Report on Conference of Molecular Spectroscopy, 1954, Institute of Petroleum.

			1 A_1 νCC		2 B_1 νCC		3 A_1 νCC		4 B_1 νCC		5 B_2 βCH		6 A_1 βCH		7 B_2 βCH		8 A_1 βCH		9 ? γCH		10 ? γCH	
			cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A
Donor–donor																						
1	NH_2	NH_2	1596	95	—		1505	200	1463	35	(—)		1150	20	—		1033	5	913	25	862	35
2	NH_2	OMe	(—)		1590 *	40	1507	300	1470 †	95	(—)		1181	80	—		1023	65	906	25	839	15
3	OMe	OMe	1594	105	—		1506	255	(—)		(—)		1176	145	—		1050	45	905	10	—	
4	CMe	OH	1619 *	40	—		1506	440	(—)		(—)		1174	50	(—)		1039	130	913	20	830	15
			1601	70									1156	25								
5	OH	OH	1613	60	—		1514	175	1472	40	(—)		1186 *	60	(—)		1028	35	916	15	861	20
													1173 *	60							845	30
Donor–halogen																						
6	NH_2	Cl	(—)		1590 *	25	1492	220	1457	75	1316 *	50	1158	30	1142	15	1023	45	—		832	10
7	NH_2	Br	(—)		1575 *	20	1486	220	1451	65	(—)		1158	30	1142	15	1015	85	—		839	5
8	OMe	Cl	1594	90	1580 *	45	1491	320	1454	80	(—)		1184	10	1132	40	1026	105	—		—	
													1162	10								
9	OMe	Br	1591	70	1580 *	40	1486	320	1452	70	(—)		1183	10	1124	30	1025 *	105	—		—	
													1163	10								
10	OH	Cl	1599	90	1590 *	60	1484	320	1465 *	35	—		1154	25	1125	25	1027	65	927	5	830	35
11	OH	Br	1602	85	1590 *	60	1479	300	1454 *	20	1323 *	20	1156	40	1115	15	1023	170	932	5	826	45
					1580 *	40																
Halogen–halogen																						
12	Cl	Cl	1576	20	—		1460	110	1438	50	1252	10	—		1126	80	1012	35	937	10	816	25
13	Cl	I	1570	25	—		1453	170	1432	65	1255	10	—		1116	30	1012	110	940	5	—	
															1103	40						
14	Br	Br	1571	25	—		1452	155	1434	50	1254	10	—		1106	90	1011	125	940	5	—	
Donor–weak																						
15	NH_2	Me	1591	40	—		1501	90	1473	70	1319 *	20	1155 *	10	—		1034	10	985	15	840	15
16	NH_2	Ph	1584 *	35	—		1503	65	1459	30	1313 *	20	1156	25	—		1045	10	990	10	850	10
17	OH	Me	1593	65	—		1495	90	1466	60	(—)		1150 *	40	(—)		1037	25	980	10	840	45
Halogen–weak																						
18	Cl	Me	1596	10	1575	20	1489 *	40	1442	30	—		—		1127	15	1040	50	—		—	
							1476	85														
19	Br	Me	1600	15	1572	25	1478 *	50	1435	25	—		—		1120	5	1044	25	996	10	830	10
							1467	90														
Weak–weak																						
20	Me	Me	1607	10	—		1498	55	1460 *	45	—		—		1118	15	1020	20	984	15	—	

			1 A_1 νCC		2 B_1 νCC		3 A_1 νCC		4 B_1 νCC		5 B_1 βCH		6 A_1 βCH		7 B_1 βCH		8 A_1 βCH		9 ? γCH		10 ? γCH	
			cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A
Donor–acceptor																						
21 NH_2	CO_2Me		1592	240	1564	130	1490	90	1458	75	(—)		1162	230	(—)		1027	15	(—)		—	
22 NH_2	NO_2		1587 *	125	1578	180	1483	40	1445	180	(—)		1168 1157 *	170 75	1105	65	1017	15	950	10	843	10
23 NH·COMe	NO_2		1613	230	1591	300	1458	150	1437	300	(—)		1164 1147	65 120	—		1040	25	956	15	831	20
24 OMe	CHO		1604	330	1589 *	60	1488	210	1443 ‡	90	(—)		1163	145	1104	50	1044	65	—		(—)	
25 OMe	NO_2		1613	200	1588	90	1493	85	1456 *	40	(—)		1184 1165	25 70	1147	25	1055 * 1045	20 35	943	10	(—)	
26 OH	CO_2Me		1618	190	1589	120	1490	300	1446 ‡	360	(—)		1160	310	(—)		1033	75	(—)		846	130
27 OH	CO_2Et		1616	195	1589	100	1489	260	(—)		(—)		1158	360	1113 *	30	1032	75	952	10	815	35
28 OH	CHO		1624	145	1584	100	1491	140	1464	165	(—)		1150	170	1114	25	1027	40	942	10	858	10
29 OH	COMe		1620	140	1584	90	1490	140	1452	165	(—)		1159	120	1129	10	1032 1022	30 25	944 *	15	834	45
30 OH	NO_2		1620	240	1593 1577 *	160 60	1479	260	1457	150	(—)		1161	60	1115 *	15	1027	60	950	10	815	25
Halogen-acceptor																						
31 Cl	CO_2Me		1596	65	1580 *	15	1478	50	1439 ‡	145	1273 *	140	1163	20	(—)		1040	50	(—)			
32 Br	CO_2Me		1594	80	1571	25	1474	60	1438 ‡	160	1270 *	150	1164	15	(—)		1044	85	(—)			
33 Cl	CHO		1595	150	1571	30	1466	40	1447	80	1291	15	1160	15	1115	15	1034	40	952	10	—	
34 Cl	NO_2		1593	105	1585 *	75	1474	60	1444	20	1260	20	—		1131	20	1035	10	949	10	—	
35 Br	NO_2		1590	110	(—)		1468	60	1438	10	1256	20	—		—		1035 †	50	945	10	—	
Weak–acceptor																						
36 CH:CH·CO_2Me	NO_2		1608	50	1576	85	1481	30	1446 *	95	1278 *	220	(—)		1142	25	1036	60	935	15	—	
37 CH:CH·CO_2Et	NO_2		1608	35	1576	50	1480	30	(—)		1275 *	130	(—)		1143 *	25	(—)		—		—	
38 CH_2Cl	CN		1606	15	—		1494	25	1458	45	1288	20	1165	5	—		—		955	10	—	
39 Me	CN		1606	30	—		1491	65	1446 *	20	1292	25	1163	15	1108	20	1043	15	947	10	—	
40 Me	CO_2Me		1604	40	1578	25	1490	35	(—)		1287 *	110	1164	25	1142 1135 *	70 65	1051	25	990	20	—	
41 Me	CO_2Et		1604	30	1578	20	1490	30	(—)		1280 *	110	1165 *	40	1142 1135 *	80 75	1051	35	999	40	—	
42 Me	NO_2		1616	55	1582	35	1486	40	1433	25	1278	20	1163	20	1148	20	1049	10	950	10	—	
Acceptor–acceptor																						
43 CO_2Me	CO_2Me		1602	45	1582	45	1491	35	1452 *	80	(—)		1165 *	20	(—)		1039	50	955 †	65	—	
44 CO_2Et	CO_2Et		1604	45	1584	45	1492	35	(—)		(—)		(—)		(—)		1040	115	958	15	—	
45 CO_2Me	NO_2		1608	35	1580	40	1485	30	1448 *	55	(—)		(—)		(—)		1036	15	(—)		(—)	
46 CHO	NO_2		1607	25	1576	55	1477 *	15	1449	40	(—)		1162 *	15	—		—		960	10	—	

* Shoulder. ‡ Peaks considered to be the superimposition of two bands. — Absence of absorption. (—) Region obscured by other absorption.
† Intensity of band increased owing to overlap of two bands.

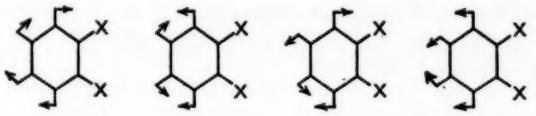
intensity can be correlated with the substituent type. The position is raised by donor substituents and lowered by halogen substituents. In general, the intensity is raised by donor or halogen substituents, as shown; but the intensity is irregular (40—300) [(170 ± 80)] in *da* compounds. In other series it has been found that donor substituents raise the intensity of the corresponding band.[1,2]

dd, dx		*xx*		*dw, xw*		*ww, xa, wa, aa*
(175—440)	>	(110—170)	>	(65—90)	>	(25—60)
[(280 ± 80)]		[(145 ± 30)]		[(80 ± 10)]		[(40 ± 15)]

The fourth band (IV) (col. 4) is found at 1473—1460 [1467 ± 6] cm.$^{-1}$ for compounds of the *dd* and *dw* classes and otherwise at 1464—1432 [1447 ± 10] cm.$^{-1}$. The intensity is high (75—300) [(170 ± 90)] for *da* compounds, but otherwise shows only random variations (10—80) [(50 ± 20)].

Randle and Whiffen reported [3] these four bands at 1609 ± 10 (var), 1575 ± 9 (var), 1490 ± 11 (s), and 1445 ± 8 (s); these positions are in good overall agreement with our more precise data.

In-plane CH-*Bending Vibrations at* ca. 1300—1000 *cm.*$^{-1}$.—Four bands corresponding to the modes (V—VIII) occur in this region. The first band (V) (col. 5) is frequently



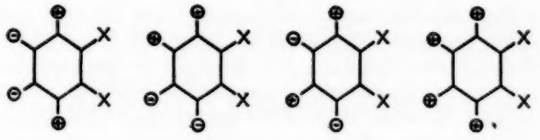
(V) (VI) (VII) (VIII)

obscured by substituent absorption, but occurs as a discrete band at 1292—1252 cm.$^{-1}$ (10—25) [1269 ± 17 cm.$^{-1}$ (15 ± 5)] in *xx*, *xa*, and *wa* compounds.

The position of the second band (VI) (col. 6) is 1168—1150 [1160 ± 4] cm.$^{-1}$ except for four compounds of the donor–donor class (Nos. 2—5) where it occurs at 1181—1174 cm.$^{-1}$. The band is absent for *xx*, *xw*, and *ww* compounds, and is of intensity (20—145) [(70 ± 45)] for *dd* compounds, (60—360) [175 ± 95] for *da* compounds, and (5—40) [(20 ± 10)] otherwise.

The third band (VII) (col. 7) is absent for compounds of the *dd*, *dw*, and *aa* classes but otherwise occurs at 1148—1103 cm.$^{-1}$ (5—65) [1125 ± 14 cm.$^{-1}$ (25 ± 15)] except that the intensity is higher (70—115) for the *xx* compounds and certain esters (Nos. 40, 41, 44).

The fourth band (VIII) (col. 8) occurs at 1056—1011 cm.$^{-1}$ (5—170) [(50 ± 40)]. The position is 1051—1034 [1040 ± 6] cm.$^{-1}$ for *dw*, *xw*, *xa*, *wa*, and *aa* compounds, 1045—1017 [1033 ± 8] cm.$^{-1}$ for *dd* and *da* compounds, and 1027—1011 [1018 ± 7] cm.$^{-1}$ for *dx*, *xx*, and *ww* compounds.



(IX) (X) (XI) (XII)

Randle and Whiffen [3] found the last three of these bands at 1159 ± 7 (m), 1126 ± 12 (m), and 1031 ± 5 (s) cm.$^{-1}$, respectively, in reasonable agreement with our results.

Out-of-plane CH-*Bending Vibrations below* 1000 *cm.*$^{-1}$.—Four modes (IX—XII) are expected. Most of the compounds show weak absorption for the 1000—900 and the 900—800 cm.$^{-1}$ region (cols. 9 and 10) which are probably due to some of these modes. For the 1000—900 cm.$^{-1}$ region most types of compound show a band at 960—935 [948 ± 7]

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cm.$^{-1}$ (10—15), but *dd* type show instead a band at 916—906 cm.$^{-1}$ (10—25), and *dw*, *xw*, and *ww* types show only a band at 996—980 cm.$^{-1}$ (10—15). About half the compounds show a band in the 900—800 cm.$^{-1}$ region.

Randle and Whiffen found [3] that the " umbrella " mode (XII) caused a strong band at 751 ± 7 cm.$^{-1}$ which would be obscured by solvent absorption in our work. They tentatively assigned bands at 977 ± 9 (w), 934 ± 11 (w), and 865 ± 14 (w) cm.$^{-1}$ to the other modes (IX—XI).

Other Bands.—Nearly all the remaining bands, $\varepsilon_A > 10$, could be assigned to substituent absorption; the following were exceptions: 1140 (45), 1070 (35) in No. 2; 1479 (50) in No. 12; 1486 (25), 1472 (35) in No. 14; 1143 (15) in No. 15; 1140 (15) in No. 16; 1340 * (35) in No. 21; 1091 (35) in No. 25.

Experimental.—The compounds were commercial products or were prepared by standard methods; all were recrystallised or distilled immediately before measurement and had melting or boiling points in agreement with values in the literature.

The spectra were measured on a Perkin–Elmer 21 Spectrophotometer with a NaCl prism and the setting previously reported.[4] ε_A values were calculated as before.[5]

This work was carried out during the tenure by one of us (R. A. J.) of a D.S.I.R. grant.

THE UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, April 9th*, 1959.]

[4] Katritzky, Monro, Beard, Dearnaley, and Earl, *J.*, 1958, 2182.
[5] Katritzky and Lagowski, *J.*, 1958, 4155.

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747. *Infrared Absorption of Substituents in Heteroaromatic Systems. Part III.*[1] *Amino-, Methylamino-, and Dimethylamino-compounds.*

By A. R. KATRITZKY and R. A. JONES.

The absorption due to the groups NH_2,NHMe, and NMe_2 for 57 compounds is recorded. Tentative assignments of the frequencies to specific molecular modes are made, and the dependence of the positions and intensities of the bands on molecular structure is discussed.

FOLLOWING our work on ethers [2] and amides,[1] we now report (Tables 1—3) the substituent absorption for amino-, methylamino-, and dimethylamino-compounds. Compounds of all these types had previously been examined, the NH stretching modes receiving most attention (for reviews see refs. 3*a* and 3*b*).

The 3300 *cm.*$^{-1}$ *Region.*—The amino-compounds show the NH antisymmetrical and symmetrical stretching bands at 3520—3420 cm.$^{-1}$ (10—80) * and 3420—3325 cm.$^{-1}$ (15—100) respectively (Table 1, cols. 1 and 2). For the *para*- and *ortho*-substituted anilines, the position of each band rises as the substituent becomes more electron-accepting; the apparent extinction coefficients also increase, those of the symmetrical vibration the more markedly. For the *meta*-substituted anilines the positions and intensities vary less; they are 3480—3430 cm.$^{-1}$ (15—35) [3458 ± 18 cm.$^{-1}$ (20 ± 8)] and 3400—3370 cm.$^{-1}$ (20—35) [3380 ±

* Round brackets signify apparent molecular extinction coefficients, and square brackets signify arithmetical means and standard deviations; see footnote on *J.*, 1959 3500.

[1] Part II, Katritzky and R. A. Jones, *J.*, 1959, 2062.
[2] Part I, Katritzky and Coats, *J.*, 1959, 2067.
[3] (*a*) Bellamy, " The Infrared Spectra of Complex Molecules," 2nd Edition, Methuen, London, 1958, pp. 248—259. (*b*) R. N. Jones and Sandorfy in Weissberger, " Techniques of Organic Chemistry, Vol. IX. Chemical Applications of Spectroscopy," Interscience, London, 1956, pp. 509—531.

10 cm.$^{-1}$ (25 ± 8)] (except that the intensities for *m*-nitroaniline are higher). These results follow the findings of earlier workers.[4-6]

For the heterocyclic compounds, the positions are in the order of electron-accepting power of the rings, *viz.*, Ph < 3P < 2P ~ 4P < 2PO.* The positions for the pyridines agree with those found by Angyal *et al.*;[7a] Goulden suggested [7b] that the measurements indicated considerable $=\overset{+}{N}H_2$ character in 2- and 4-amino-pyridine. Mason [8] recently related the positions and intensity of these bands for heterocyclic amines with their molecular structure. The intensities are higher for 4- than for 3-amino-pyridine; the pyridine ring is known to withdraw electrons more readily from the 4- than the 3-position of the ring. The relatively low extinction coefficients for 2-aminopyridine and its 1-oxide are probably connected with the intramolecular hydrogen bonding in these compounds;[9,10] the ε_A values for the other heterocyclic compounds are probably affected by intermolecular hydrogen bonding (the values found by Mason [8] in dilute solution were considerably higher). In general, despite the sodium chloride prism (poor resolution) and the use of a standard concentration, our results are in reasonable agreement with others: *e.g.*, aniline showed bands at 3454 cm.$^{-1}$ (23) and 3388 cm.$^{-1}$ (30) in chloroform with a calcium fluoride prism;[11] the intensities were *ca.* (25) and (30),[3b] (20) and (28),[4] and *ca.* (30) and (35) [4b] in carbon tetrachloride (lithium fluoride prism).

For the methylamino-compounds the position of the NH stretch (Table 2, col. 1) at 3450—3420 cm.$^{-1}$ also becomes higher as the ring becomes more electron-accepting:[12] Ph < 3P < 4P ~ 4PO. The position is relatively low in the 2-substituted pyridine and its 1-oxide, although these rings are strongly electron-accepting,[12] probably because of internal hydrogen bonding. 4-Methylaminopyridine 1-oxide shows (in 0·2M-solution) an additional band at 3240 cm.$^{-1}$ (75) due to the intramolecularly hydrogen-bonded species (cf. discussion in ref. 10). For methylaniline 3430 cm.$^{-1}$ [13] and 3433 cm.$^{-1}$ (39) [14] were previously given.

The 2800 *cm.*$^{-1}$ *Region.*—The symmetrical CH stretching frequency (possibly perturbed by Fermi resonance) reported [15] for compounds with NMe or NMe_2 groups directly attached to an aromatic system at *ca.* 2800 cm.$^{-1}$ (30—70) is found (Table 2, col. 2; Table 3, col. 1) at 2870—2800 cm.$^{-1}$ (25—60). It is more distinct for compounds with rings of low electron-attracting power (phenyl, substituted phenyl, and 3-pyridyl) in agreement with previous work,[15] *e.g.*, the band is absent for *N*-methylamides,[1,15b] in which a strongly electron-attracting group is attached to the nitrogen atom.

The 1650—1480 *cm.*$^{-1}$ *Region.*—The NH_2 scissor deformation is shown at 1632—1613 [1622 ± 4] cm.$^{-1}$ (Table 1, col. 3) except for 2-aminopyridine 1-oxide where strong intramolecular hydrogen bonding apparently shifts the mode to *ca.* 1590 cm.$^{-1}$. For the *para*-substituted compounds, increase in the electron-attracting character of the substituent raises frequencies somewhat (1613→1628 cm.$^{-1}$) and intensities markedly (60→420). *ortho*-Substituted compounds show a similar intensity variation (95 → 440) but the positions are more constant at 1626—1616 cm.$^{-1}$ [1620 ± 3]. For the *meta*-substituted anilines the positions and intensities vary less: 1632—1620 cm.$^{-1}$ (175—260) [1623 ± 3 cm.$^{-1}$ (220 ± 30)]. As expected, the intensity is higher for 4- than for 3-aminopyridine; the intensities

* P = pyridyl; PO = pyridine oxide.

[4] Califano and Moccia, *Gazzetta*, (*a*) 1956, **86**, 1014; (*b*) 1957, **87**, 58; (*c*) 1957, **87**, 805.
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TABLE 1. *Amino-compounds.*

		1		2		3		4		Note
		NH_2 stretch				NH_2 def.		CN stretch		*a*
		antisym.		sym.						
		cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	
para-*Substituted anilines* (*substituent is given*)										
1	NMe_2	3420	20	3380	20	1614	75	1260	90	*h*, *i*
2	OMe	3450	15	3380	15	1615	60	(—)		*h*, *j*
3	OEt	3430	20	3380	25	1613	60	(—)		*h*, *j*
4	Me	3420	10	3360	15	1623	125	1262	65	*h*
5	Cl	3430	20	3380	25	1621	160	1270	80	*h*
6	Br	3430	15	3370	25	1620	150	1270	90	*h*
7	4P §	3480 *	20	3400	45	1627	310	($CHCl_3$)		
8	3P	3480	15	3400	45	1625	260	1280	140	*h*
9	2P	3480	15	3410	35	1628	275	1284	95	*e*, *h*
10	2PO §	3450 *	25	3380	60	1620	340	($CHCl_3$)		
11	N:NPh	3500	20	3400	70	1624	340	1291	155	*h*
12	CN	3480	35	3380	70	1622	340	1303	105	*h*
13	CO_2Et	3480	25	3390	70	1623	410	(—)		*h*
14	COMe	3470	25	3380	55	1620	420	(—)		*h*
15	NO_2	3520	35	3420	90	1627	350	(—)		*h*
meta-*Substituted anilines*										
16	NH_2	3430	30	3380	40	1620	330	1319	70	*h*
17	OMe	3450	15	3380	20	1624	260	1329 1313 *	55 40	*j*, *h*
18	OEt	3460	10	3370	20	1622	220	1326 1310 *	55 40	*j*, *h*
19	Me	3430	20	3380	25	1622	185	1306 * 1288	20 60	*h*
20	Cl	3470	25	3380	35	1623	250	1318 1260	20 50	*h*
21	Br	3470	25	3380	35	1621	250	1315 1257	25 45	*h*
22	4P	3460	15	3380	25	1622	230	1315	50	*h*
23	2P	3470	15	3390	25	1623	175	1320	90	*e*, *h*
24	2PO	3450 *	15	3370	20	1622	190	1320 1296	60 40	*h*
25	CF_3	3470 *	20	3400	35	1628	190	1317 *	110	*h*
26	NO_2	3480	35	3390	55	1632	260	1332 * 1265	135 70	*h*
ortho-*Substituted anilines*										
27	NH_2	3400	*45*	3325	*35*	1622	*190*	1276	*175*	*l*
28	OMe	3445	25	3370	30	1616	200	(—)		*l*
29	Cl	3460	30	3385	35	1619	250	1308 1263	70 15	*l*
30	Br	3450	25	3370	30	1618	260	1311 1260	70 10	*l*
31	Me	3450	15	3380	20	1623	160	1304 1272	40 45	
32	Ph	3450	20	3370	25	1617	210	1297 1285 *	65 60	*l*
33	CO_2Me	3470	45	3370	50	1617	260	1317 *	110	*l*
34	NO_2	3515	80	3390	100	1626	440	1288 1260	180 460	*l*
Aniline and heterocyclic amines (*ring is given*)										
35	Ph	3455	20	3375	25	1622	185	1268	55	*g*
36	4P ∞	3480	30	3400	45	1625	310	1314 1254	45 35	*d*
37	3P	3460	20	3380	25	1622	125	1282 1250	60 50	*f*
38	2P	3470	20	3390	35	1614 ‡	465	1317 1250	90 40	*e*
39	2PO	3500	25	3360	20	1592 *	45	1340 1255 *	25 25	*c*

TABLE 2. *Methylamino-compounds.*

		1		2		3		4		5		6		7		8		9		10
		NH stretch		N–Me		NH in plane def.		N–Me Me sym. bend.		N–Me Me antisym. bend		Ring–N CN stretch				N–Me Me rock		N–Me CN stretch		
No.	Ring	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	*a*
1	Ph	3420	30	2820	25	1478	50	(—)		1425	30	1320	110	1263	75	1154	45	1065 *	20	*g*
2	4P	3460	45	2850 *	40	1480	35	1460	30	1417	20	1342	75	1315	80	1152	20	1068	35	
3	3P	3430	30	2825	30	1500	110	1460	45	1408	40	1340 *	15	1302	70	1149	40	1069	10	*f*
												1317 *	55							
4	2P	3440	30	(—)		(—)		1457	40	1410 *	55	1324	45	1285	55	1152	50	1070	15	
5	4PO	3450	55	(—)		1498 *	120	1456 *	20	(—)		1335	25	1308	15	1155	50	1065	35	*b*
6	2PO	3340	40	(—)		—		(—)		1419	35	1336	25	1267 *	20	1157 ‡	150	1070	35	*c*

TABLE 3. *Dimethylamino-compounds.*

		1		2		3		4		5		6		7		8		Note
		NMe_2		Me bend		Ring–N CN stretch		?		NMe_2 Me rock				NMe_2 C–N–C stretch antisym.		sym.		*a*
No.	Ring	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	
1	$C_6H_4{\cdot}NH_2$-*p* [n]	2870	60	1448	45	1332	60	(—)		1158	75	1137	70	1051	25	942	60	*i*, *h*
		2800	60															
2	Ph	2870	50	1444	50	1343	105	(—)		1189	35	1130	30	1057	40	943	40	*g*
3	$C_6H_4{\cdot}CH{:}CHPh$-*p*	2810	55	1449	105	1360	240	—		1187	130	1130	65	1063	35	946 §	105	
4	$C_6H_4{\cdot}[CH{:}CH{\cdot}4P]$-*p*	2810 *	45	($CHCl_3$)		1357	240	1330 *	100	1154	75	1124	55	1061	35	944	80	
5	$C_6H_4{\cdot}[CH{:}CH{\cdot}4PO]$-*p*	2820 *	60	(—)		1359	220	1330 *	70	(—)		(—)		1058	40	945	75	*h*
6	$C_6H_4{\cdot}NO_2$-*p*	2820 *	40	1442	80	1372	100	(—)		1173 *	60	(—)		1061	55	943	90	*h*
7	4P	2840 *	45	1448	95	1380	155	1346	35	1179	35	1108	30	1063	35	951	55	*d*
8	3P	2810	25	1446	45	1358	90	1320	35	1169	35	(—)		1063	10	944	20	
								1306	40									
9	2P	2820 *	20	(—)		1369	40	1318	35	1174	20	—		1053	15	953	25	
10	4PO	(—)		1447 ‡	165	1379	70	1326	35	1181 *	120	(—)		1063	25	952	105	*b*
11	2PO	2820 *	50	1444 ‡	150	1356	125	—		1176 ‡	280	1143 ‡	95	1055 ‡	60	952	170	*c*

* Shoulder. ‡ Peaks considered to be formed by the super-imposition of two bands. — Absence of absorption. (—) Region obscured by other absorption. ($CHCl_3$) region obscured by solvent. § Measured in 1 mm. cell because of poor solubility.

Ph phenyl; P substituted pyridine; PO substituent pyridine 1-oxide (position of substituent denoted by a numeral).

(*a*) Many other bands found in the compounds have been published by Katritzky and his co-workers in the following papers: *J.*, 1958, (*b*) p. 2192, (*c*) p. 2195, (*d*) p. 2198, (*e*) 2202, (*f*) p. 3165, (*g*) p. 4155; *J.*, 1959, (*h*) p. 2051, (*i*) this paper, (*j*) p. 2062, (*k*) p. 2058, (*l*) preceding paper. (*m*) Extra band at 839 (40). (*n*) Extra band at 1475 (45).

of the heterocyclic compound are probably not directly comparable with the benzenoid compound because of intramolecular hydrogen bonding. This band has been previously reported at 1640—1560,[3b,16,17] and at 1650—1590 cm.$^{-1}$.[3a] Eight aromatic amines were shown [4] to absorb at 1631—1615 cm.$^{-1}$ (s).

A band at 1500—1478 cm.$^{-1}$ (35—110, but apparently absent in No. 6) for the methylamino-compound (Table 2; col. 3) is possibly the NH in-plane deformation, to which Hadži and Škrbljak [18] assigned a band near 1500 cm.$^{-1}$ for secondary aromatic amines.

The 1460—1400 *cm.*$^{-1}$ *Region.*—The methylamino-compounds show bands at 1460—1457 cm.$^{-1}$ (30—45) [1459 ± 2 cm.$^{-1}$ (40 ± 10)] and 1425—1408 cm.$^{-1}$ (20—40) [1417 ± 7 cm.$^{-1}$ (30 ± 10)] (Table 2, cols. 4 and 5). These are assigned to the antisymmetrical and symmetrical *N*-methyl CH bending modes, respectively. The positions are higher than those [1422 ± 4, 1369 ± 11 cm.$^{-1}$] for amides of the type Ar·NMe·CO·R,[1] but close to those 1465—1442, 1414—1401 cm.$^{-1}$ for amides R·CO·NHMe.[19]

The dimethylamino-compounds absorb at 1449—1442 cm.$^{-1}$ (45—95) [1446 ± 3 cm.$^{-1}$ (70 ± 20)] (Table 3, col. 2); this is probably also a methyl CH bending mode.

The 1400—1240 *cm.*$^{-1}$ *Region.*—Previous work [17,3a] had indicated that the CN stretching mode caused absorption at 1340—1250, 1350—1280, and 1360—1310 cm.$^{-1}$ for primary, secondary, and tertiary aromatic amines, respectively. Six aromatic amines absorbed [4c] at 1288—1276 cm.$^{-1}$ but *m*-chloro- and *m*-bromo-aniline each showed three bands at 1320—1261 cm.$^{-1}$. A band at 1262—1241 cm.$^{-1}$ in seven secondary aromatic amines was assigned [18] to this mode, but the published curves all show a second band at higher frequencies.

All the compounds now studied show one or two strong or medium bands (Table 1, col. 4; Table 2, cols. 6, 7; Table 3, col. 3) which are assigned to the *N*-ring CN stretching mode.

The position of the band should depend on the electron-accepting character of the ring; when this is increased, greater mesomerism, greater double-bond character, and therefore a higher frequency, should result. This is shown for the *para*-substituted anilines (Table 1, nos. 1—15) for which the frequency varies, 1260—1303 cm.$^{-1}$; the intensity is (65—155) [(105 ± 30)].

The *meta*-substituted anilines (except for the methyl, and possibly the nitro-compounds) show a band at 1329—1315 [1320 ± 6] cm.$^{-1}$ (20—90) [(50 ± 20)]; for several compounds a second band is shown at a lower frequency; this is similar to the ring-oxygen stretching frequency in *meta*-substituted anisoles and phenetoles;[2] the reason is unknown. As expected, the aminopyridines and 1-oxides all absorb at higher frequencies than aniline (Table 4), the intensity is (25—90); a weaker band at 1254—1250 cm.$^{-1}$ is also shown.

For the dimethylamino-compounds, the band occurs at 1380—1332 cm.$^{-1}$; for corresponding pairs, 16—76 [55 ± 23] cm.$^{-1}$ higher than in the amino-compounds. The intensity is (40—155) [(95 ± 35)] except in the vinyl compounds (Nos. 3—5) where it is (220—240). For the benzenoid compounds a *para*-amino-group lowers the frequency and *para*-vinyl and -nitro-groups raise it as expected. All the heterocyclic compounds absorb at higher frequencies than dimethylaniline (Table 4).

Two bands of comparable intensity at 1342—1320 and 1315—1263 cm.$^{-1}$ are shown for all the methylamino-compounds; presumably the CN stretching mode is split by interaction with another mode. The mean frequency has been taken as that for the CN stretching mode; it is 20—50 [35 ± 15] cm.$^{-1}$ higher than that for the corresponding amino-compound, and higher for each heterocyclic compound than for methylaniline (Table 4). Each component of the doublet has an intensity of (45—110) [(75 ± 15)] in methylamino-benzene and -pyridine, but (15—25) in methylaminopyridine 1-oxides.

[16] Thompson, *J.*, 1948, 328.
[17] Colthup, *J. Opt. Soc. Amer.*, 1950, **40**, 397.
[18] Hadži and Škrbljak, *J.*, 1957, 843.
[19] Miyazawa, Shimanouchi, and Mizushima, *J. Chem. Phys.*, 1956, **24**, 408; *J. Chem. Soc. Japan*, 1956, **77**, 171.

The increments in Table 4 (except those for 2-methylaminopyridine and its 1-oxide; these exceptions are possibly explained by proximity effects) indicate that the electron-accepting power of the various rings is in the order: Ph < 3P < 4PO ~ 4P ~ 2P < 2PO, which is in good agreement with other evidence.[2]

TABLE 4. *Nitrogen-ring stretching bands. Increments in wave-numbers over those for the corresponding benzenoid compound.*

	4P	3P	2P	4PO	2PO
Amino	46	14	49	—	72
Methylamino [a]	37	18	13	30	10
Dimethylamino	37	15	26	36	64

[a] Mean frequency of doublet used, see text.

The 1200—1100 *cm.*$^{-1}$ *Region.*—A band (Table 2, col. 8) for the methylamino-compound at 1157—1149 cm.$^{-1}$ (20—50) [1153 ± 2 cm.$^{-1}$ (40 ± 15)] and two bands (Table 3, cols. 5 and 6) for the dimethylamino-compounds at 1189—1154 cm.$^{-1}$ (20—130) [1171 ± 14 cm.$^{-1}$ (60 ± 35)] and 1143—1108 cm.$^{-1}$ (30—70) [1126 ± 10 cm.$^{-1}$ (50 ± 20)] (absent in No. 9) are probably due to *N*-CH_3 methyl rocking frequencies by analogy with those found for *N*-methylamides.[1]

The 1100—900 *cm.*$^{-1}$ *Region.*—For dimethylamine the CNC antisymmetric and symmetric stretching modes occur at 1082 and 930 cm.$^{-1}$.[20] Bands probably due to these modes are found for the dimethylamino-compounds at 1063—1051 cm.$^{-1}$ (15—55) [1059 ± 4 cm.$^{-1}$ (35 ± 15)] and 953—942 cm.$^{-1}$ (25—170) [947 ± 4 cm.$^{-1}$ (75 ± 45)] (Table 3, cols. 7, 8). For certain amidines containing the ·NMe_2 group these bands were found [21] at 1082—1081 (ms) and 947—936 (m) cm.$^{-1}$.

For the methylamino-compounds a band tentatively assigned to the *N*-methyl CN stretching frequency (Table 2, col. 9) is found at 1070—1065 cm.$^{-1}$ (10—35) [1068 ± 2 cm.$^{-1}$ (25 ± 15)]; Hadži and Škrbljak found [18] this band near 1060 cm.$^{-1}$ and suggested that it was the CN stretching or the *N*-Me rocking mode. The NH_2 wagging mode [4c] near 1050 cm.$^{-1}$ is apparently too weak to be detected under our conditions.

Other Bands.—Nearly all the remaining bands could be assigned to the ring or other substituents present; many of them have been published, and references are given in Tables 1—3. The small proportion of bands which could not be correlated are given as footnotes in Tables 1—3.

Experimental.—See Part I [2] for details.

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[20] Edsall, *J. Chem. Phys.*, 1937, **5**, 225.
[21] Fabian, Delaroff, and Legrand, *Bull. Soc. chim. France*, 1956, 287.

748. N-*Oxides and Related Compounds. Part XVI.*[1] *Infrared Spectra of 3-Substituted Pyridine 1-Oxides.*

By A. R. Katritzky, J. A. T. Beard, and N. A. Coats.

The positions and intensities of ten characteristic bands are recorded and discussed for nineteen 3-substituted pyridine 1-oxides. The preparation of several new oxides is described.

Previous Parts have recorded the spectra of 2-[2] and 4-substituted pyridine 1-oxides;[3] we now report on some 3-analogues. For reasons which have been given[4] the spectra were measured at 0·2M concentration in purified chloroform in a 0·117 mm. cell and apparent molecular extinction coefficients were recorded. The errors and approximations involved therein have been noted,[4] as has the reproducibility to be expected on different machines under these conditions.[5] The infrared spectra of eleven 3-substituted pyridine 1-oxides (variously in CCl_4, $CHCl_3$, CS_2, or as mulls) have been discussed by Shindo;[6] this work is compared with ours below.

The 3000 cm.$^{-1}$ *Region.*—The hydrogen-bonded chloroform CH stretching frequency (cf. refs. 1, 2) is found at 3020—2965 cm.$^{-1}$ (70—170) [2985 ± 15 cm.$^{-1}$ (120 ± 30)].*

Ring CC *and* CN *Stretching Frequencies in the* 1600—1400 *cm.*$^{-1}$ *Region.*—The four bands expected in this region are found (Table 1, cols. 2—5) at 1612—1598 [1605 ± 4] cm.$^{-1}$, 1570—1558 [1565 ± 3] cm.$^{-1}$, 1490—1468 [1480 ± 6] cm.$^{-1}$, and 1440—1425 [1434 ± 5] cm.$^{-1}$ (except that the final band absorbs at 1417 in the 3-phenyl-compound). These positions agree reasonably well with those found by Shindo:[6] 1610—1587, 1573—1538, 1499—1471 and 1456—1427 cm.$^{-1}$.

The intensities of the first three of these bands depend on the nature of substituent (electron-donor substituents increasing the intensity) but the intensity of the fourth band varies comparatively little (Table 2). These intensity variations have already been discussed and correlated with the symmetry of the particular vibration and the charge distribution in the ring.[7]

N^+–O^- *Stretching Band.*—This is found at 1308—*ca.* 1230 cm.$^{-1}$ (Table 1, col. 6). The intensity is (185—370) [(275 ± 65)]. The position of the band rises in general with increasing electron-acceptor properties of the substituent, but detailed correlation is difficult for the band is split into two components in the methyl-, chloro-, cyano-, and nitro-derivatives and is overlapped by strong substituent absorption in the carbonyl compounds.

CH *In-plane Bending Modes.*—Of the four possible modes of this type, only one is identified at 1160—1150 [1156 ± 2] cm.$^{-1}$ (Table 1, col. 8). The intensities depend on the electron-donor power of the substituent: OR (390—400) > Me (290) > unsaturated carbon (220—230) > chloro (70) > strong electron-acceptors (30—45) except that the cyano- (185) and phenyl compound (125) are respectively stronger and weaker than expected. This mode was found by Shindo[6] at 1191—1153 (m—s) and probably corresponds to that in *meta*-disubstituted benzenes at [1157 ± 5] cm.$^{-1}$,[8] the intensity of which

* Parentheses enclose apparent extinction coefficients; square brackets enclose arithmetical means and standard deviations. The position of shoulders and the intensity of shoulders and superimposed bands were not used in the statistical treatment.

[1] Part XV, Katritzky, Monro, and Beard, *J.*, 1958, 3721.
[2] Katritzky and Hands, *J.*, 1958, 2195.
[3] Katritzky and Gardner, *J.*, 1958, 2192.
[4] Katritzky, Monro, Beard, Dearnaley, and Earl, *J.*, 1958, 2182.
[5] Katritzky and Lagowski, *J.*, 1958, 4155.
[6] Shindo, *Chem. Pharm. Bull. Japan*, 1958, **6**, 117; 1956, **4**, 460.
[7] Katritzky, *J.*, 1958, 4162.
[8] Katritzky and Simmons, *J.*, 1959, 2058

TABLE 1.

No.	Substituent	$CHCl_3$ νCH		A_1 νCC / νCN		B_1 νCC / νCN		A_1 νCC / νCN		B_1 νCC / νCN		ν^+N-O^-		?		B_1 βCH		B_1 Ring		B_2 γCH		A_2 γCH		
		cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	
1	OEt	2970	140	1602	115	1565	170	1490	175	1440	130	($CHCl_3$)		1179	280	1156	400	1011	80	993	95	843	30	*b*
																				987*	60			
2	OMe	2970	120	1605	150	1566	175	1488	170	1438†	160	(1238	100)	1190	135	1169	170	1008	140	965	115	844	30	*b*
																1150	390							
3	Me	2970	125	1608	85	1568	20	1482	90	1428	65	1278	215	1165*	170	1158	290	1017	125	946	75	891	15	—
												1268	190											
4	CH_2CO_2Et	2980	150	1610	95	1560	25	1485	100	1440†	240	1270	370	($CHCl_3$)		1156†	350	1019	160	982	100	874	35	*c*
5	Ph	2980	115	1606	115	1564	45	1472†	120	1417	115	1308	185	1190	100	1160	125	1015	135	900	175	870	45	*d*
6	$CH{:}CHCO_2Et$	2975	105	1602	110	1563	35	1484	130	1433	155	1262	330	($CHCl_3$)		1157	230	1015	120	(—)		857	70	*c*
7	$CH{:}CHCO_2Pr^n$	2975	145	1598	90	1562	30	1482	105	1430	130	1262	320	(—)		1155	230	1015	160	990*	55	855	60	*e*
8	$CH{:}CHCO_2Bu^n$	2965	170	1600	80	1558	25	1482	100	1432	140	1261	330	(—)		1155	220	1015	140	(—)		856	55	*e*
9	Cl	3000	90	1600	120	1565	15	1470	160	1426	175	1293	175	—		1155	70	1015	145	917	275	853	50	—
												1260	195											
												1250*	150											
10	CN	3020	70	1605	85	1560	25	1477	75	1425	115	1307	220	—		1153	185	1015	190	958	110	868	55	*f*
												1290	230											
11	CO_2Me	3120	30	1610	75	1570	35	1482	60	1442†	270	1307†	570	($CHCl_3$)		1158	40	1017	175	997	115	890	35	*c*
		3010	105																					
12	CO_2Et	2980	85	1602	45	1566	20	1475	50	1436	165	1298†	560	—		1156	40	1014†	230	952	60	889	25	*c*
13	CO_2Pr^n	2975	135	1608	45	1568	20	1480	60	1437	170	1296†	500	—		1158	40	1015	165	966	90	889	40	*e*
14	CO_2Pr^i	2995	125	1610	50	1568	25	1480	55	1436	180	1296†	510	1180*	50	1158	35	1016	170	961	165	890	25	*e*
15	CO_2Bu^n	2980	145	1607	50	1565	20	1477*	45	1435	160	1295†	510	—		1154	35	1014	160	957	65	888	25	*e*
16	CO_2Bu^i	2995	165	1612	45	1566	20	1480*	55	1437	175	1296‡	480	($CHCl_3$)		1158	35	1016	150	985	135	888	35	*e*
17	CO_2Bu^s	2980	150	1609	45	1568	25	1480	60	1436	180	1297†	480	1172*	35	1157	35	1015	175	956	105	888	30	*e*
18	COMe	2990	90	1606	45	1561	25	1477	20	1433	145	1280	280	—		1159	45	1014	125	925	30	896	70	*c*
19	NO_2	2970	70	1620*	15	(—)		1468	90	1440	160	1290	300	—		1154	30	1012	190	949	65	873	70	*f*
												1257	260											

* Shoulder. † Peak considered to be formed by the superimposition of two bands. ‡ Peak strongly overlapped by neighbouring band. (—) Band is masked by stronger absorption. — Absence of band; ($CHCl_3$) Band is masked by solvent absorption.

Extra bands that could not be correlated with the substituent were found for: No. 1 at 894 cm.$^{-1}$ (20), No. 3 at 1306 (55) and 855 cm.$^{-1}$ (20), No. 11 at 903 cm.$^{-1}$ (55), No. 18 at 871 cm.$^{-1}$ (30).

a This column gives cross references to substituent bands, details of which have been published: *b* Katritzky and Coats, *J.*, 1959, 2062. *c* Ref. 4. *d* Ref. 5. *e* Katritzky, Beard, and Lagowski, in preparation. *f* Katritzky, unpublished work.

TABLE 2. *Intensities of ring stretching frequencies at* 1600—1400 *cm.*$^{-1}$.

Nos. in Table 1	Substituent type	Band near 1605		Band near 1565		Band near 1480		Band near 1434	
		Range	Mean and deviation	Range	Mean and deviation	Range	Mean and deviation	Range	Mean and deviation
1—2	Donor	115—150	130	170—175	170	170—175	170	130	130
3—9	Weak	80—120	100 ± 15	15—45	30 ± 10	90—160	115 ± 25	65—175	130 ± 40
10—19	Acceptor	45—85	55 ± 15	20—35	25 ± 5	20—90	60 ± 20	115—180	160 ± 20
1—19	All substituents	45—150	80 ± 35	15—175	40 ± 50	20—175	95 ± 45	65—180	150 ± 30

varies with substituents in much the same way. As in the *meta*-benzenes, this band often shows a shoulder or subsidiary band at higher frequencies (col. 9).

Ring Breathing Mode.—This (col. 9) occurs at 1019—1008 cm.$^{-1}$ (80—190) [1015 ± 2 cm.$^{-1}$ (150 ± 25)]; the corresponding mode occurs at [995 ± 3 cm.$^{-1}$ (20 ± 15)] in *meta*-benzenes.[8] Shindo reported [6] this band at 1022—1008 cm.$^{-1}$ (m—s).

Out-of-plane CH *Bending Frequencies.*—Two of these modes are probably represented by the bands listed in Table 1, cols. 10 and 11. The position of the first mode is very variable 997—900 [957 ± 27] cm.$^{-1}$, the intensity is (30—270) [(110 ± 55)]; it probably corresponds to that absorbing at [914 ± 8 cm.$^{-1}$ (20 ± 10)] for *meta*-benzenes. The second band of intensity (15—70) [(40 ± 15)], is found at 844—843 cm.$^{-1}$ for the alkoxy-compounds (Nos. 1, 2), at 857—853 cm.$^{-1}$ for the unsaturated esters (Nos. 6—9) and otherwise at 896—868 [884 ± 9] cm.$^{-1}$; for *meta*-benzenes the corresponding band absorbs at [836 ± 5] cm.$^{-1}$ for the compounds with two donor-substituents and at [880 ± 11] cm.$^{-1}$ otherwise.

Absorption which sometimes occurs just above the solvent cut-off at 805 cm.$^{-1}$ is probably a third out-of-plane mode, reported by Shindo [6] at 817—743 cm.$^{-1}$. We find

TABLE 3. *Esters.*

		Found			Quoted			
Ester *	Yield	B. p.	mm.	n_D †	B. p.	*mm.*	n_D †	Ref.
3Py·CO_2Pr^n	81	138·5—139·5°	25	1·4984(18·5)	134°	23	1·4964(25)	*a*, *b*
3Py·CO_2Pr^i	33	125—127	30	1·4931(18·5)	131	27	—	*b*
3Py·CO_2Bu^n	68	144	20	1·4950(19)	130	11	1·4933(25)	*a*, *b*
3Py·CO_2Bu^i	57	126	17	1·4950(14·5)	110—111	8	—	*b*
3Py·CO_2Bu^s	50 ‡	101·5	0·3	1·4816(16)	—	—	—	
3Py·CH:CH·CO_2Pr^n	45 §	172	25	1·5504(15)	—	—	—	
3Py·CH:CH·CO_2Bu^n	50 ¶	173—174	15	1·5450(17·5)	—	—	—	

* 3Py denotes 3-pyridyl radical. † Temperature of determination given in parentheses. [a] Badgett, Provost, Ogg, and Woodward, *J. Amer. Chem. Soc.*, 1945, **67**, 1135. [b] Charront, Harispe, Harispe, and Chevillard, *Bull. Soc. chim. France*, 1948, 1014. ‡ Found: C, 66·6; H, 7·5; N, 7·7. $C_{10}H_{13}O_2N$ requires C, 67·0; H, 7·3; N, 7·8%. § Found: C, 69·0; H, 7·0; N, 7·5. $C_{11}H_{13}O_2N$ requires C, 69·1; H, 6·8; N, 7·3%. ¶ Found: C, 70·1; H, 7·6; N, 7·1. $C_{12}H_{15}O_2N$ requires C, 70·2; H, 7·4; N, 6·8%.

TABLE 4. *3-Substituted pyridine 1-oxides.*

Subst.	M. p.	Crystal form	Yield (%)	Solvent	*a*	Formula or lit. m. p.	Found (%) / Required (%) C	H	N
CO_2Pr^n	49—50·5°	rhombs	71	Pet.	D, E	$C_9H_{11}O_3N$	59·6	6·2	—
							59·7	6·1	—
CO_2Pr^i	70	cubes	82	EtOAc	—	$C_9H_{11}O_3N$	59·5	6·2	7·7
							59·7	6·1	7·7
CO_2Bu^n	30—33	plates	48	[b]	D, E	$C_{10}H_{13}O_3N$	62·1	6·6	6·9
							61·5	6·7	7·2
CO_2Bu^i	62—62·5	rhombs	62	EtOAc	D	$C_{10}H_{13}O_3N$	62·0	6·8	7·2
							61·5	6·7	7·2
CO_2Bu^s	43—46	—	49	[c]	D, E	$C_{10}H_{13}O_3N$	61·2	6·4	7·3
							61·5	6·7	7·2
CH:CH·CO_2Pr^n	89—91	rhombs	70	EtOAc	—	$C_{11}H_{13}O_3N$	63·7	6·6	6·6
							63·7	6·3	6·8
CH:CH·CO_2Bu^n	69—71	rhombs	93	EtOAc	D, E	$C_{12}H_{15}O_3N$	64·9	6·8	6·2
							65·1	6·8	6·3
CN	174—175	—	47	EtOH	—	175—176 [d]	—	—	—
Cl	57—58	cubes	80	C_6H_6	D	C_5H_4ONCl	46·6	3·1	—
							46·3	3·1	—
NO_2	169—169·5	yellow needles	40	EtOH	—	$C_5H_4O_3N_2$	43·1	2·6	—
						167—169 [e]	42·9	2·9	—
Me	37—38	—	—	[f]	D, E	33—36 [f]	—	—	—

* In this column D indicates that the compound was deliquescent, E that the m. p. was determined in an evacuated tube. [b] Distilled, b. p. 146—148°/0·15 mm.; Jaffe and Doak, *J. Amer. Chem. Soc.*, 1955, **77**, 4441, give b. p. 135—139°/0·16 mm., but no m. p. [c] Distilled, b. p. 180·5/2 mm. [d] Jujo, *J. Pharm. Soc. Japan*, 1946, **66**, 21; *Chem. Abs.*, 1951, **45**, 6200. [e] Ochiai and Kaneko, *Pharm. Bull. Japan*, 1957, **5**, 56. [f] Hevy and Tsai, *J. Amer. Chem. Soc.*, 1954, **76**, 4184. [g] Distilled, b. p. 114—115°/1·5 mm. Pet = light petroleum, b. p. 60—80°.

absorption for Nos. 1, 2, 12, 13, 14, 15, 19 at respectively 819 (35), 828 (55), 822 (35), 807 (45), 805 (30), 805 (25), 818 cm.$^{-1}$ (250).

Substituent Bands.—All the remaining bands in the spectra with $\varepsilon_A > 10$ of these compounds could be assigned to substituent absorption (the few exceptions are given in footnotes to Table 1). Many of them have been published; cross references are given in col. 12.

Preparation of Compounds.—The following compounds have already been described (Nos. refer to Table 1); Nos. 4, 12, 18; [9] No. 5; [10] No. 6; [11] No. 11.[4] The other compounds were prepared by standard methods as indicated in the Experimental section.

Experimental

Esters of Nicotinic Acid.—Thionyl chloride (11·9 g.) was added with stirring below 0° to nicotinic acid (12·3 g.) under pyridine (16 c.c., previously dried by successive treatment with KOH pellets and freshly calcined CaO). The whole was then stirred for 1½ hr. at 100°, the alcohol (0·1 mole) added, and the heating continued for 3 hr. more. The mixture was added to water (160 c.c.) and just basified with aqueous ammonia (*d* 0·088). Ether-extraction (3 × 50 c.c.) gave, from the dried ($MgSO_4$) extracts, the ester by distillation. Details are given in Table 3.

Esters of β-Pyridylacrylic Acid.—The acid (10 g.), alcohol (25 c.c.), and sulphuric acid (10 c.c.) were heated for 18 hr. at 100°. The mixture was worked up as above. Details of the *products* are given in Table 3.

Conversion of Pyridines into their N-Oxides.—The pyridine (0·01 mole) in acetic acid (6 c.c.) and 30% aqueous hydrogen peroxide (1·5 c.c.) was heated at 70° and volatile material then removed to 100°/20 mm. The residue in chloroform (5 c.c.) was treated with potassium

Table 5. *Picrates.*

Base †	M. p.	Crystal form	Formula or lit. m. p.	Found (%) C	H	N	Required (%) C	H	N
3PyCO$_2$Pr^n	129—130°	—	129·5—130° [a]	—	—	—	—	—	—
3PyO·CO$_2$Pr^n	91·5—92	prisms	$C_{15}H_{14}O_{10}N_4$	44·2	3·3	13·8	43·9	3·4	13·7
3Py·CO$_2$Pr^i	145·5	rhombs	$C_{15}H_{14}O_9N_4$	46·1	3·6	14·3	45·7	3·6	14·2
3Py·CO$_2$Bu^n	113—114	—	113·5—114° [a]	—	—	—	—	—	—
3PyO·CO$_2$Bu^n	84—85·5	needles	$C_{16}H_{16}O_{10}N_4$	45·3	3·7	13·3	45·3	3·8	13·2
3Py·CO$_2$Bu^i	124	needles	$C_{16}H_{16}O_9N_4$	47·2	3·8	—	47·1	3·9	—
3PyO·CO$_2$Bu^i	90	prisms	$C_{16}H_{16}O_{10}N_4$	45·7	3·9	13·5	45·3	3·8	13·2
3Py·CO$_2$Bu^s	99·5—100·5	needles	$C_{16}H_{16}O_9N_4$	47·0	3·9	13·7	47·1	3·9	13·7
3PyO·CO$_2$Bu^s	94·5—95·5	rhombs	$C_{16}H_{16}O_{10}N_4$	45·3	3·7	12·9	45·3	3·8	13·2
3Py·CH:CH·CO$_2$Pr^n	128—128·5	prisms	$C_{17}H_{16}O_8N_4$	48·6	3·9	13·0	48·6	3·8	13·3
3Py·CH:CH·CO$_2$Bu^n	100	rods	$C_{18}H_{18}O_8N_4$	49·9	4·2	13·3	49·8	4·2	12·9
3PyO·CH:CH·CO$_2$Bu^n	109—110	rhombs	$C_{18}H_{18}O_{10}N_4$	47·8	3·8	12·8	48·0	4·0	12·4
3PyO·Me	149—151	plates	$C_{12}H_{10}O_9N_4$ 138—139° [b] 141—143° [c]	42·9	3·0	16·2	42·6	3·0	16·6
3PyO·OMe	155—156	needles	$C_{12}H_{10}O_9N_4$	41·1	3·0	15·6	40·7	2·8	15·8
3PyO·OEt	125—125·5	needles	$C_{13}H_{12}O_9N_4$	43·0	3·4	14·9	42·5	3·3	15·2

† 3Py indicates 3-substituted pyridine ring, 3PyO indicates 3-substituted pyridine 1-oxide ring.
[a] Footnote *a* of Table 3. [b] Bockelheide and Linn, *J. Amer. Chem. Soc.*, 1954, **76**, 1290. [c] Footnote *f* of Table 4.

carbonate (2 g.) and the oxide recovered from the filtered solution by evaporation. Details are recorded in Table 4. 3-Ethoxy-, m. p. 85—86°, b. p. 175° (bath)/0·05 mm. and 3-methoxypyridine 1-oxide, m. p. 100—101°, were prepared by refluxing 3-chloropyridine 1-oxide overnight with the corresponding alcoholic sodium alkoxide: they were characterised as picrates (Table 5), prepared in and recrystallised from ethanol.

Part of this work was done during the tenure (by A. R. K.) of an I.C.I. Fellowship.

The Dyson Perrins Laboratory, Oxford.
The University Chemical Laboratory, Cambridge. [*Received, May 15th*, 1959.]

[9] Katritzky, *J.*, 1956, 2404.
[10] Hands and Katritzky, *J.*, 1958, 1754.
[11] Katritzky and Monro, *J.*, 1958, 150.

749. *The Structures of Dicyclopentadienyl-tin and -lead.*

By L. D. Dave, D. F. Evans, and G. Wilkinson.

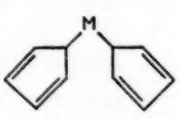
Infrared, nuclear magnetic resonance, ultraviolet, and dipole-moment measurements have been made on the dicyclopentadienyl-tin and -lead compounds and their methyl-substituted derivatives. The structures of these compounds are discussed and evidence for an angular sandwich structure is presented.

The cyclopentadienyl-tin(II) [1] and -lead(II) [2] compounds $(C_5H_5)_2Sn$ and $(C_5H_5)_2Pb$ were prepared by Fischer and his co-workers, who suggested for them the σ-bonded structure (I); this suggestion was supported by the dipole moments of the compounds,[3] the values being $\mu[Sn(C_5H_5)_2] = 1{\cdot}02 \pm 0{\cdot}06$ D and $\mu[Pb(C_5H_5)_2] = 1{\cdot}63 \pm 0{\cdot}06$ D, it being taken that $P_A = 0{\cdot}1P_E$.

That the σ-bonded structure was unlikely was shown by the measurements of their infrared spectra in carbon tetrachloride solution by Lindstrom and Barusch.[4] The remarkable similarity of these spectra to that of ferrocene led these workers to conclude that the tin and lead compounds had similar sandwich-bonded or π-cyclopentadienyl rings bound to the metal atom. Since such a conclusion could be reconciled with the dipole-moment evidence, if correct, only by assuming that the two metal–ring bonds were at an angle (II), it seemed desirable to confirm the published data and obtain additional evidence.

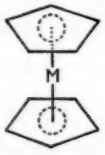
Infrared Spectra.—The spectra have been measured, in a vacuum, in solution in carbon disulphide and tetrachloroethylene; measurements were also initially made in carbon tetrachloride but, as a slow chemical reaction sets in, this solvent was less suitable. The results are given in Table 1, together with those for ferrocene [5] for comparison. The recent measurements of the infrared spectra of these compounds, reported by Fritz,[6] are so much at variance with the solution data given here and previously [4] that they can only be considered as unreliable. The discrepancy is probably due to the difficulty of preparing halide discs of these air-sensitive substances without extensive decomposition.

The close similarity of the infrared spectra of the tin and lead compounds to each other and to ferrocene is thus confirmed, showing that the three compounds have a basically similar (sandwich) structure. However, there are two possibilities for the tin and the lead cyclopentadienyls: an axial sandwich structure of the ferrocene type (III) and an



(I)

(II)



(III)

angular sandwich structure (II). It is theoretically possible to distinguish between the two possible structures from the infrared studies. The axial sandwich belongs to the D_{5d} group whereas the angular one has a much lower symmetry, *viz.*, C_{2v}, the rings being assumed to be freely rotating. From the similarity of the infrared spectra, it might appear that the tin and lead compounds have a ferrocene-like structure. However, the local symmetry of each delocalised ring (D_{5h}) is the same for both types of structure and hence the ring vibrations, *e.g.*, the C–H stretch or bend, C–C stretch, etc., would be very similar.

[1] Fischer and Grubert, *Z. Naturforsch.*, 1956, **11***b*, 423.
[2] Fischer and Grubert, *Z. anorg. Chem.*, 1956, **286**, 237.
[3] Weiss, *ibid.*, 1956, **287**, 236.
[4] Lindstrom and Barusch, 131st Amer. Chem. Soc. Meeting, Miami, 1957, Abstract 77.
[5] Lippincott and Nelson, *Spectrochim. Acta*, 1958, **10**, 307.
[6] Fritz, *Chem. Ber.*, 1959, **90**, 780.

The presence of the central metal atom can affect the infrared spectrum in the following ways:

(1) For D_{5d} symmetry, which is higher than D_{5h}, the selection rules will be more stringent and fewer vibrations will be infrared-active. For C_{2v} symmetry, on the other hand, the symmetry becomes lower and hence more vibrations will appear in the infrared region. A comparison of the infrared spectra of the tin and the lead compound on the one

TABLE 1. *Infrared spectra of cyclopentadienyl-tin and -lead, with sodium chloride optics unless otherwise stated.*

$Sn(C_5H_5)_2$		$Pb(C_5H_5)_2$		$Fe(C_5H_5)_2$ [a]
C_2Cl_4	CS_2	C_2Cl_4	CS_2	
3100 [b] s(sh.)	3100 [b] s(sh.)	3090 [b] s(sh.)	3090 [b] s(sh.)	3085 s
3094 [b] s	3094 [b] s	3082 [b] s	3082 [b] s	3075 m(sh.)
2919 [b] w	2918 [b] w	2917 [b] w	2917 [b] w	
2695 w	2695 [b] w	2680 w		
2280 w		2278 w		
2210 w		2200 w		
2085 w		2080 w		
			1745 m	1758 m
1750 m	1750 m	1732 m	1720 m	1720 m
1632 m				1684 m
				1650 m
		1622 m		1620 m
1532 m		1515 m		
1482 w		1482 w		
1426 s		1427 s		1411 s
	1360 m		1351 m	
	1340 m			
1260 w	1260 w	1255 w	1260 w	
1228 w	1228 w	1228 w	1228 w	
	1193 vw		1190 vw	1188 w
	1156 w		1156 w	
	1112 s		1113 s	1108 s
			1082 vw	
1055 w	1055 w	1055 w	1052 w	1051 w
	1002 s		1005 s	1002 s
				834 w
	805 w		805 w	
	780 m		780 w	
	748 vs		750 vs	811 s
666 [c] w	666 w	666 [c] w	666 w	782 w
				492 s
				478 s

[a] See Ref. 5. [b] Measurements using calcium fluoride prism and 1·0 mm. silica cell. [c] No new bands found from 700 to 400 cm.$^{-1}$ in tetrachloroethylene solution with potassium bromide optics.

hand and ferrocene on the other shows several weak bands in the former that are not observed in the latter, consistently with the lower symmetry.

(2) More striking differences can be expected for the metal–ring stretches. Lippincott and Nelson [5] considered ferrocene as a linear XY_2 molecule so that only the asymmetric stretch is infrared-active; they assigned the band at 478 cm.$^{-1}$ to this vibration. Since an angular sandwich may, similarly, be considered as an angular triatomic molecule, XY_2, both the symmetric and the asymmetric vibrations should be infrared-active. Since the tin and the lead compound are thermally less stable than ferrocene, it seems likely that the metal–ring stretches would here lie below that in ferrocene (478 cm.$^{-1}$). No new bands in the region 700—400 cm.$^{-1}$ were observed and the metal–ring stretches probably lie at still lower frequencies. The very strong band in the spectra of both the tin and the lead compound at *ca.* 750 cm.$^{-1}$ is too high to be a metal–ring stretch. We assign it as a C–H bend ($\perp$) which would correspond to the similar 811 cm.$^{-1}$ and 773 cm.$^{-1}$ bands in ferrocene and nickelocene, respectively.[5]

The infrared spectra of the di(methylcyclopentadienyl)-tin and -lead compounds were

also measured from 4000—400 cm.$^{-1}$. They are, in general, similar to those of the dicyclopentadienyl-tin and -lead except for the presence of vibrations due to the methyl groups.

Nuclear Magnetic Resonance Studies.—The high-resolution nuclear magnetic resonance spectra of $Sn(C_5H_5)_2$ and $Pb(C_5H_5)_2$ show only one main proton line at 175 c./sec. and 193 c./sec., respectively, relative to cyclohexane on the low-field side. A sandwich structure, with rings freely rotating as in ferrocene,[7] gives only one line. The σ-bonded structure (I) would be expected to give a complicated line spectrum owing to the non-equivalence of the five protons on each ring. Such a line pattern is not always found in σ-compounds, however. Thus, π-C_5H_5-(σ-C_5H_5)$Fe(CO)_2$ gives only two lines,[7] one assigned to protons in the π-C_5H_5 ring and the other in the σ-C_5H_5 ring. Similarly, we found that $Hg(C_5H_5)_2$ which, on the basis of its complex infrared structure, is assigned a σ-bonded linear structure,[8] shows, even under very high resolution, only one proton line, as also observed by Strohmeier and Lemmon.[9]

In the tin compound the main proton line has two weaker lines symmetrically disposed about it at a separation of $\pm$15·9 c./sec. Each of these lines is a doublet with a separation of about 0·36 c./sec. These lines presumably arise from those molecules in the mixture which contain the tin isotopes ^{117}Sn (abundance = 7·67%; spin = $\frac{1}{2}$; $\mu = -0{\cdot}9949$ nuclear magnetons) and ^{119}Sn (abundance = 8·68%; spin = $\frac{1}{2}$; $\mu = -1{\cdot}040$ nuclear magnetons). The presence of a nuclear species with spin of $\frac{1}{2}$ would produce a doublet splitting of the resonance of the protons bound to it by electron-pair bonds through indirect spin–spin coupling interaction. The magnitude of this splitting for these two tin isotopes should be in the ratio of their magnetic moments since the chemical bonding is the same; in fact, the observed ratio of the splitting is 0·977 which is, within the limits of error, the same as the ratio $\mu(^{117}Sn)/\mu(^{119}Sn) = 0{\cdot}956$. Similar weak lines could not be detected with $Pb(C_5H_5)_2$ although lead has one isotope, ^{207}Pb, which has abundance = 20·82%, spin = $\frac{1}{2}$, and $\mu = 0{\cdot}5837$ nuclear magnetons. Thus the nuclear magnetic resonance spectra of $Sn(C_5H_5)_2$ and $Pb(C_5H_5)_2$ are consistent with a sandwich structure, but a localised σ-bonded structure cannot be ruled out on this basis alone.

The nuclear magnetic resonance spectra of $Sn(CH_3{\cdot}C_5H_4)_2$ and $Pb(CH_3{\cdot}C_5H_4)_2$ show only two main lines with intensity ratio 5 : 3. If these methyl derivatives were mixtures of several σ-bonded isomers with the methyl group on $C_{(1)}$, $C_{(2)}$, or $C_{(3)}$, a very complicated spectrum would be expected. If only one particular σ-structure was energetically favoured, even then a mutual splitting of the ring and methyl proton lines may be expected. This splitting would be expected for a sandwich structure also. In the latter case, however, the splitting may be extremely small, as in the analogous case of toluene where only two proton lines, one due to the methyl and the other due to the phenyl hydrogen atoms, are observed under normal resolution. Hence the absence of splitting on the two proton lines in these methyl derivatives is consistent with a sandwich structure but does not completely rule out the localised σ-bonded structure.

Dipole Moments.—A decision between the two types of sandwich structure could be made on the basis of dipole-moment measurements. Weiss [3] has determined the moments of cyclopentadienyl-tin and -lead in benzene solution. Since benzene is known, in certain cases, to form polar charge-transfer complexes,[10] and as these compounds are easily decomposed in solution by traces of oxygen, it was thought desirable to determine the dipole moments in a different solvent. In carbon disulphide, we find for $Sn(C_5H_5)_2$, $\mu = 0{\cdot}96 \pm 0{\cdot}06$ D and for $Pb(C_5H_5)_2$, $\mu = 1{\cdot}49 \pm 0{\cdot}06$ D, P_A being taken as 0·1 P_E as was done by Weiss.[3] Our results are thus in fair agreement with those of Weiss. While the present work was in progress, the dipole moments, in cyclohexane, have been reported.[11] The

[7] Piper and Wilkinson, *J. Inorg. Nuclear Chem.*, 1956, **3**, 104.
[8] Piper and Wilkinson, *ibid.*, 1956, **2**, 82.
[9] Strohmeier and Lemmon, *Z. Naturforsch.*, 1959, **14***a*, 109.
[10] Mulliken, *J. Amer. Chem. Soc.*, 1952, **74**, 811; Orgel, *Quart. Rev.*, 1954, **8**, 422.
[11] Fischer and Schreiner, *Chem. Ber.*, 1959, **90**, 938.

values obtained were $\mu(Sn) = 0.96 \pm 0.10$ D and $\mu(Pb) = 1.29 \pm 0.04$ D. In view of the different solvent, these values are also consistent with ours.

It is unlikely that the above values of dipole moments can be explained by a large atom polarisation, (P_A), especially in view of the fact that other non-polar cyclopentadienyl compounds have low values of P_A.[11] Even in $Mg(C_5H_5)_2$, where the metal–ring bonds are very polar,[12] P_A is only 31·1% of P_E.[11] Hence we conclude that both these tin and lead compounds have permanent dipole moments.

Visible and Ultraviolet Spectra.—The spectra are given in Table 2. The compounds show, in the ultraviolet region, a band not found in any di-π-cyclopentadienyl metal compound (*e.g.* of V,[13] Cr,[13] Fe,[14] Co,[13] or Ni[13]) or metal cyclopentadienides (Mg,[13] Mn[13]).

These bands show slight " blue shifts " (not very pronounced in the case of the tin compounds) in going from 2,2,4-trimethylpentane to the polar tetrahydrofuran. The

TABLE 2. *Absorption spectra.*

	$Sn(C_5H_5)_2$		$Sn(CH_3{\cdot}C_5H_4)_2$		$Pb(C_5H_5)_2$	
Solvent	$\lambda_{max.}$	ε	$\lambda_{max.}$	ε	$\lambda_{max.}$	ε
2,2,4-Trimethylpentane	295	4270	305	3600	343	7460
Tetrahydrofuran	293	4300	303	4850	335	7600

spectra were measured up to 220 mμ but in view of the ready hydrolysis of these compounds by even traces of water the results were not considered reliable below 280 mμ and hence are not given.

Nature of Bonding.—The infrared and the dipole-moment evidence shows clearly that these compounds have angular sandwich structures; nuclear magnetic resonance spectra are consistent with such a formulation. Such a sandwich structure is the first of its kind known and presents an interesting problem as regards bonding. A simple way of considering the bonding is to regard both $Sn(C_5H_5)_2$ and $Pb(C_5H_5)_2$ as similar to the gaseous stannous and plumbous halides which also have angular structures.[15] The tin and lead atoms may be considered to be in an sp^2 hybrid state. Two hybrid orbitals each containing one electron can then overlap with one orbital of each ring containing one electron to form two single covalent bonds inclined to each other. The third sp^2 hybrid orbital then contains the remaining two electrons as a lone pair. Complete hybridisation may not, of course, occur and the lone pair may have more *s* character and the bonding orbitals more *p* character. The same angular structure would be expected from considerations of electrostatic repulsion between the bonding and the non-bonding electrons.[16] Furthermore, an axial sandwich of the ferrocene type is unlikely since such a structure with linear *sp* hybrid bonds would have the two non-bonding electrons in the degenerate p_z and p_y orbitals. According to Hund's rule, the ground state would be a triplet which is, of course, not observed.

As regards the cyclopentadienyl ring orbitals, the five π electrons can be assigned to the molecular orbitals, a_1, e_1, and e_2, in that order of energy.[17] The electron distribution in its ground state, therefore, is a_1^2, e_1^3, e_2^0. As a_1 is the only orbital with the right symmetry to combine with the hybrid metal orbital, for bonding to occur, one electron from a_1 must be promoted to e_1. This partly filled a_1 ring π-orbital can then overlap the metal orbital to give a σ-bond. Since this ring a_1 orbital is " hollow " (it follows the ring framework and is antisymmetrical to it), its overlap with the metal orbitals is not likely to be efficient, which may explain, in part, the comparative thermal instability of these compounds.

[12] Wilkinson, Cotton, and Birmingham, *J. Inorg. Nuclear Chem.*, 1956, **2**, 95.
[13] Dave and Wilkinson, unpublished results.
[14] Kaplan, Kester, and Katz, *J. Amer. Chem. Soc.*, 1952, **74**, 5531.
[15] Lister and Sutton, *Trans. Faraday Soc.*, 1941, **37**, 406.
[16] Gillespie and Nyholm, *Quart. Rev.*, 1958, **11**, 339.
[17] Moffitt, *J. Amer. Chem. Soc.*, 1954, **76**, 3386.

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There is also a possibility of secondary π-bonding between the doubly filled four e_1 orbitals of the two rings and the empty p_z and d orbitals of the metal. This will impart some multiple-bond character to the metal–ring bonds but will not affect the free rotation of the two rings as there are two identical e_1 orbitals at right angles to each other on each ring.

Experimental

Preparation of Compounds.—$Sn(C_5H_5)_2$ and $Pb(C_5H_5)_2$ were prepared by the general method of reaction of sodium cyclopentadienide with anhydrous metal salts in tetrahydrofuran.[12,18] High yields were obtained and this procedure was more convenient than those given previously.[1,2] Anhydrous stannous chloride and lead chloride were normally used. Lead acetate, dehydrated by azeotropic distillation with excess of benzene, gave better yields than lead chloride, presumably owing to its higher solubility in the solvent. Lead nitrate, as recommended by Fischer and Grubert,[2] should be avoided as it can lead to violent explosions during sublimation.

The methylcyclopentadienyl compounds were prepared by a similar method from sodium methylcyclopentadienide.[19] The *tin* derivative (Found: Sn, 43·7. $C_{12}H_{14}Sn$ requires Sn 42·88%) is a pale yellow (almost colourless) liquid at room temperature. The *lead* compound (Found: Pb, 57·0. $C_{12}H_{14}Pb$ requires Pb, 56·7%) is a low-melting yellow solid. The lead compound, in the liquid state, readily supercools. The properties of these methyl derivatives are, in general, similar to those of the cyclopentadienyl compounds; they are, however, less stable than the latter to heat and, as expected, to air also.[19]

Solvents.—Contrary to published statements,[1,2] the tin and lead compounds were found to be very sensitive to traces of moisture in the solvents. For all physical measurements except the ultraviolet spectrum, drying over phosphoric oxide or lithium aluminium hydride for *ca.* 3—4 hr. was adequate. For ultraviolet measurements, such a drying of spectroscopically pure solvents always resulted in slightly turbid solutions. It was found necessary to dry (P_2O_5 or $LiAlH_4$) for at least 24 hr. in a vacuum, accompanied by frequent magnetic stirring. During this period the rest of the vacuum line was evacuated and heated. The solvents for all spectral measurements were deoxygenated by cooling in liquid air and evacuating repeatedly. These measurements were repeated after recrystallising the compounds in a vacuum from " AnalaR " light petroleum and resubliming them.

Apparatus and Instruments.—Infrared measurements were made on a Perkin-Elmer Model 21 spectrophotometer with CaF_2, NaCl, and KBr optics. A vacuum cell made of a metal framework to which the appropriate windows were cemented with Araldite and fitted with a copper-to-glass seal was used. The path length was 1·5 mm. The nuclear magnetic resonance spectra were measured at 40 Mc./sec. on a Varian Associates Model 4300B spectrometer with super-stabiliser. The samples, together with a cyclohexane capillary as external reference, were contained in 5-mm. o.d. sample tubes which were sealed in a vacuum. Dipole-moment measurements were made at 25° ± 0·1° on a heterodyne-beat capacitance meter similar to that described by Sutton and Hill [20] with a modified Sayce–Briscoe [21] type cell. All operations were carried out in an atmosphere of dry nitrogen. Visible and ultraviolet spectral measurements were made on a Perkin-Elmer Spectracord 4000 using 1·0 and 10·0 mm. silica cells sealed in a vacuum.

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[18] Wilkinson, *Org. Synth.*, 1956, **36**, 31.
[19] Reynolds and Wilkinson, *J. Inorg. Nuclear Chem.*, 1959, **9**, 86.
[20] Sutton and Hill, *J.*, 1953, 1482.
[21] Sayce and Briscoe, *J.*, 1925, **127**, 315.

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750. *The Effect of Pressure on the First Dissociation Constant of "Carbonic Acid."*

By A. J. Ellis.

The apparent first dissociation constant of "carbonic acid" has been determined for pressures up to 3000 atm. in the temperature range 25—65° c. An increase of 2500 atm. increases this constant approximately ten-fold owing largely to the increased hydration of carbon dioxide to H_2CO_3 at high pressure.

The effects of pressure on the molar conductances of potassium chloride, hydrochloric acid and potassium hydrogen carbonate in water at these temperatures are compared with previous results. There is little change in the effects of pressure in the concentration range 0·0001—0·1M.

As only 0·259% of the equilibrium mixture, $CO_2 + H_2O$, or "carbonic acid," is hydrated to H_2CO_3 in water at 25°,[1] increased pressure influences two equilibria

$$H_2O + CO_2 \rightleftharpoons H_2CO_3; \quad H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$$

For comparison, the effects of pressure on the dissociation of simple weak acids such as formic, acetic, propionic acid, are available from the reviews of Cohen and Schut,[2] and Hamann.[3]

Davies's method [4] was used to obtain the acid dissociation constants for "carbonic acid" between 25° and 65°, and at various pressures. The degree of dissociation, α, of the mixture $CO_2 + H_2O$ into H^+ and HCO_3^- ions was assumed to equal the ratio Λ/Λ', where Λ is the molar conductance of the mixture and Λ' the sum of the molar conductances of the ions H^+ and HCO_3^- at the ionic strength of the solution examined. Λ' was obtained by interpolation of conductance values for hydrochloric acid, potassium chloride, and potassium hydrogen carbonate solutions at various concentrations, temperatures, and pressures. As indicated by Hamann [3] it is safe to assume that Kohlrausch's law of independent ionic mobilities is obeyed under the conditions used.

The thermodynamic apparent dissociation constant K_a is given on the molal scale by the expression

$$K_a = [\alpha^2 m/(1 - \alpha)]\gamma_\pm^2/\gamma_{HA}$$

where m is the molal concentration of total carbon dioxide, and $\gamma_\pm$ the mean activity coefficient of the H^+ and the HCO_3^- ion. γ_{HA}, the activity coefficient of the undissociated acid, was taken as unity at all pressures and temperatures. Values for $\gamma_\pm$ were obtained from the Debye–Hückel equation in the form

$$-\log f_\pm = \{1{\cdot}8123 \times 10^6(DT)^{-3/2}c^{\frac{1}{2}}\}/\{1 + 50{\cdot}29 \times 10^8(DT)^{-\frac{1}{2}}ac^{\frac{1}{2}}\}$$

a was taken as 5×10^{-8} cm., and changes of the molar concentration c and the dielectric constant D with pressure were taken into consideration. At the low ionic strengths used, the molar activity coefficient $f_\pm$ can be taken as equal to the molal activity coefficient $\gamma_\pm$. As the term DT changes little with temperature in the range 25—65°, it was sufficient for the accuracy of the experiments to apply the 25° values of $\gamma_\pm$ for various pressures and concentrations at all the temperatures.

A comparison of Hamann's results [3] with earlier data [2,5] for the conductance of strong electrolytes in water at high pressures showed that there were appreciable deviations and

[1] Wissbrun, French, and Patterson, *J. Phys. Chem.*, 1954, **58**, 693.
[2] Cohen and Schut, "Piezochemie Kondensierter Systeme," Akademische Verlagsgesellschaft m.b.H., Leipzig, 1919.
[3] Hamann, "Physico-chemical Effects of Pressure," Butterworths, London, 1957.
[4] Davies, *J. Phys. Chem.*, 1925, **29**, 977.
[5] Zisman, *Phys. Review*, 1932, **39**, 151.

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these are discussed below in relation to the values obtained for solutions of potassium chloride and hydrochloric acid in the process of obtaining dissociation constants.

Experimental

Apparatus.—The stainless-steel pressure vessel (25 c.c.; 3 in. diam.) had two manganin wire electrical leads through its walls; these were insulated in a packing gland of compressed polystyrene. Into the vessel was placed the conductivity cell containing the solution, and the appropriate electrical leads were soldered together inside the vessel.

The conductivity cell (constant 0·365 cm.$^{-1}$) was a Teflon cylinder, open at one end, of 7 c.c. capacity. A tight-fitting Teflon piston supporting the electrodes separated the solution in the cell from medicinal paraffin used to transmit pressure within the pressure vessel. The electrode assembly in the cell consisted of platinum foil electrodes tightly bound by fine platinum wire to the arms of a U-shaped Pyrex glass piece. A thick platinum lead from one electrode supported the assembly from the Teflon piston, and a lead of fine wire from the other electrode to the piston allowed for the slight play caused by the contraction of Teflon under pressure. The cell therefore incorporated the advantages of the sliding piston design of Jamieson,[6] and almost constant spacing of the electrodes by glass. The platinum in the cell was lightly coated with platinum black.

Sealed platinum-in-glass electrodes are usually broken by the application of a few thousand atm. pressure. In cells with electrodes spaced by plastic, corrections are needed for the high and often irreproducible compressibility of these substances. For example, a marked discontinuity is apparent in the conductivity results of Hamann and Strauss [7] at 5000 atm. where Weir [8] reported a phase change in Teflon with a 2% decrease in volume. Disadvantages of other cells used previously include direct contact of the solution with kerosene [5] and with mercury.[9]

Pressures were developed by hand hydraulic pumps and a pressure intensifier. Bourdon gauges were calibrated against a Harwood manganin-coil resistance gauge supplied calibrated to $\pm$0·1%. With allowance for small variations in the Bourdon gauges, the pressures reported should be accurate to within $\pm$0·5%.

The pressure vessel and a paraffin reservoir were heated in an oil-bath controlled to $\pm$0·05°. The mass of the vessel damped out temperature variations in the bath. About 2 hr. were required for the apparatus to reach initial thermal equilibrium, and a further 30 min. were required after a change of pressure for equilibrium to be regained.

The resistances were measured with a capacity-compensated non-inductive Wheatstone bridge using a 1000 c.p.s. valve oscillator as an A.C. source. Corrections to the conductances were made for the resistance of lead wires and the change in cell constant with pressure. The latter was 0·1% change per 1000 atm.

Measurements of the cell resistance were taken again at 1 atm. pressure at the end of each run. In no case were hysteresis effects important.

Materials and Method.—Solutions of potassium chloride, hydrochloric acid and potassium hydrogen carbonate were prepared from "AnalaR" reagents. A large volume of "carbonic acid" solution was prepared in a closed flask, and the liquid and the gas phase were allowed to equilibrate. A portion of this solution was run into the conductance cell, and another portion analysed.

Throughout the experiments with "carbonic acid" the pressure on the cell was kept above 50 atm. to prevent bubbles forming in the cell. A short extrapolation was made to get conductances at 1 atm. No significant amount of carbon dioxide was lost from the cell during the measurements.

The distilled water in the cell was assumed to have two types of impurity, *viz.*, carbon dioxide and stray strong electrolyte ions. The conductance blank due to the latter, κ_i changes very little with pressure, while that of ionised carbonic acid, κ_c, increases considerably. From the conductance of the solvent at various pressures it was possible to obtain the values of κ_i and κ_c. As an example, for the water used in the experiment at 25° and 1 atm., κ_i was approximately $1{\cdot}0 \times 10^{-6}$ and κ_c $0{\cdot}5 \times 10^{-6}$ ohm^{-1} cm.$^{-1}$.

[6] Jamieson, *J. Chem. Phys.*, 1953, **21**, 1385.
[7] Hamann and Strauss, *Trans. Faraday Soc.*, 1955, **51**, 1684.
[8] Weir, *J. Res. Nat. Bur. Stand.*, 1953, **50**, 95; 1954, **53**, 245.
[9] Buchanan and Hamann, *Trans. Faraday Soc.*, 1953, **49**, 1425.

When corrections for the solvent were made to the conductances of potassium chloride solutions ($\kappa_l + \kappa_c$) was subtracted, but for hydrochloric acid and potassium hydrogen carbonate only the blank κ_l, for pressure and temperature, was applied.

The correction for solvent conduction was of the order of a few units % for solutions with an ion concentration of 10^{-3}m, but reached a maximum of 20% of the total conduction for 10^{-4}m potassium chloride at 25° and 3000 atm. The blank correction to the "carbonic acid" conductivities was greatest at 65° and 1 atm. where it amounted to about 10%.

TABLE 1.

P (atm.)	500	1000	1500	2000	2500	3000
ρ_t	1·021	1·039	1·058	1·073	1·088	1·103

TABLE 2. *Hydrochloric acid: values of* $\Lambda^P\rho_t/\Lambda^1$ (*M = molar concentrations at $P = 1$*).

(Owen and Sweeton's values [11] of Λ^1 in parentheses.

	M	1	500	1000	2000	3000
25°	0·1	(391·3)	1·050	1·088	1·152	1·193
	0·01	(412·0)	1·051	1·089	1·152	1·191
	0·01	(421·4)	1·050	1·087	1·151	1·191
	0·0001	(424·7)	1·05	1·10	1·16	1·21
35°	0·1	(447·3)	1·040	1·074	1·127	1·164
	0·01	(472·3)	1·041	1·075	1·128	1·162
	0·001	(483·3)	1·041	1·070	1·126	1·165
	0·0001	(487·0)	1·04	1·09	1·14	1·18
45°	0·1	(502·2)	1·034	1·068	1·120	1·158
	0·01	(530·5)	1·034	1·066	1·118	1·156
	0·001	(544·2)	1·033	1·067	1·117	1·154
55°	0·1	(554·0)	1·032	1·062	1·112	1·148
	0·01	(586·5)	1·032	1·063	1·113	1·149
	0·001	(602·3)	1·033	1·065	1·115	1·150
65°	0·1	(603·0)	1·031	1·060	1·105	1·142
	0·01	(640·5)	1·030	1·060	1·106	1·140
	0·001	(657·5)	1·029	1·062	1·108	1·142

Values of $\Lambda_0{}^P/\Lambda_0{}^1$ *for hydrochloric acid solutions.*

Temp.	P (atm.) 1	500	1000	2000	3000
25°	(426·2)	1·028	1·048	1·074	1·080
35	(489·2)	1·020	1·034	1·051	1·056
45	(550·3)	1·013	1·027	1·042	1·048
55	(609·5)	1·012	1·025	1·039	1·043
65	(666·8)	1·009	1·022	1·032	1·035

TABLE 3. *Potassium chloride: values of* $\Lambda^P\rho_t/\Lambda^1$.

(Λ^1 values in parentheses up to 45° from Gunning and Gordon,[12] and at 55° and 65° from the present work.)

	M	P (atm.) 1	500	1000	2000	3000
25°	0·1	(129·0)	1·031	1·052	1·069	1·061
	0·01	(141·3)	1·031	1·052	1·068	1·058
	0·001	(147·0)	1·032	1·054	1·069	1·064
	0·0001	(149·3)	1·03	1·06	1·08	1·07
35°	0·1	(154·7)	1·023	1·044	1·052	1·044
	0·01	(169·9)	1·024	1·040	1·049	1·042
	0·001	(176·9)	1·025	1·04(5)	1·05(5)	1·05(0)
45°	0·1	(180·3)	1·020	1·038	1·044	1·030
	0·01	(199·7)	1·021	1·035	1·040	1·026
	0·001	(208·1)	1·02(0)	1·03(5)	1·04(1)	1·03(0)
55°	0·1	(208·3)	1·015	1·026	1·035	1·023
	0·01	(230·1)	1·017	1·028	1·033	1·021
	0·001	(241·0)	1·02	1·03(1)	1·04(0)	1·03(0)
65°	0·1	(235·5)	1·014	1·026	1·026	1·011
	0·01	(262·3)	1·015	1·025	1·027	1·012
	0·001	(278·2)	1·01(5)	1·02(3)	1·02(6)	1·01(7)

Values of $\Lambda_0{}^P/\Lambda_0{}^1$ *for* KCl *solutions.*

($\Lambda_0{}^1$ values to 45° from Gunning and Gordon [12] in parentheses.)

Temp.	P (atm.) 1	50	1000	2000	3000
25°	(149·9)	1·011	1·014	0·996	0·964
35	(180·5)	1·004	1·004	0·979	0·947
45	(212·5)	1·000	0·997	0·971	0·931
55	(246·0)	0·996	0·989	0·965	0·927
65	(281·3)	0·994	0·987	0·957	0·917

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Buchanan and Hamann [9] defined the molal conductance of an electrolyte as Λ (molal) = $1000L'/m$, where m is the molality of the electrolyte, which is independent of pressure, and L' the specific conductance of the solution corrected for the solvent blank.

At low ionic strengths the following approximate relation holds, Λ (molal) = Λd, where d is the density of the solution. This equation is valid at all concentrations used in the present experiments within the possible experimental error.

In this work the product Λd is used instead of the term molal conductance, as the former emphasises that the increase in conductance with pressure is due to both a volume factor and one involving the mobility of the ions.

The results are reported as the ratios $\Lambda^P\rho_r/\Lambda^1$ where Λ^P and Λ^1 are the molar conductances of the electrolytes at a pressure P and at 1 atm., respectively. ρ_r is the corresponding density ratio ρ^P/ρ^1 for water at the temperature. Values of ρ_r taken from Dorsey [10] and given in Table 1 represent the solution densities within $\pm 0{\cdot}2\%$ in the temperature range 25—65°.

Electrolyte solutions ranging from 0·1 to 0·0001M were examined up to 3000 atm. at temperatures between 25° and 65°. The results for 10^{-4}M-solutions were of little significance above 35° because of the high solvent correction to the conductances.

Tables 2 to 4 give, in order, the change in conductivity with pressure for solutions of hydrochloric acid, potassium chloride, and potassium hydrogen carbonate. Table 5 gives the change in conductivity for water in equilibrium with the cell assembly.

The values of $\Lambda^P\rho_r/\Lambda^1$ did not change significantly with concentration in the range 0·1—0·0001M. At the end of each of the Tables 2—4 values for the ratio $\Lambda^P{}_0/\Lambda^1{}_0$ are given for the electrolytes. To obtain these values it was assumed that the effects of pressure on conductance remained constant down to infinitely small electrolyte concentrations.

TABLE 4. *Potassium hydrogen carbonate: values of* $\Lambda^P\rho_r/\Lambda^1$.

(Λ^1 values in parentheses based on Shedlovsky and MacInnes's results [13] up to 40°, and the present work.)

	M		P (atm.)					M		P (atm.)			
		1	500	1000	2000	3000			1	500	1000	2000	3000
25°	0·1	(97·7)	1·025	1·041	1·050	1·034	45°	0·1	(138)	1·014	1·020	1·021	1·004
	0·01	(110·1)	1·026	1·042	1·048	1·031		0·01	(155·0)	1·013	1·022	1·023	1·002
	0·001	(115·3)	1·024	1·041	1·049	1·033		0·001	(163·5)	1·115	1·024	1·025	1·005
	0·0001	(117·3)	1·03	1·05	1·06	1·04							
35°	0·1	(118)	1·019	1·031	1·034	1·019	55°	0·1	(158)	1·012	1·016	1·014	0·994
	0·01	(131·8)	1·018	1·030	1·033	1·017		0·01	(178·5)	1·010	1·015	1·012	0·992
	0·001	(139·2)	1·020	1·032	1·032	1·016		0·001	(189·0)	1·014	1·014	1·015	0·996
							65°	0·1	(181)	1·008	1·013	1·002	0·986
								0·01	(202·8)	1·007	1·010	1·004	0·984
								0·001	(189·0)	1·009	1·012	1·004	0·987

Values of $\Lambda_0{}^P/\Lambda_0{}^1$ *for* $KHCO_3$ *solutions.*

Temp.	P (atm.)	1	500	1000	2000	3000
25°		(118·0)	1·005	1·002	0·978	0·937
35		(141·5)	0·999	0·992	0·963	0·922
45		(179·3)	0·993	0·985	0·954	0·909
55		(192·8)	0·989	0·977	0·944	0·901
65		(219)	0·987	0·974	0·936	0·894

TABLE 5. *The effect of pressure on the conductance of the distilled water used in the experiments: Typical values of specific conductivity* $\times 10^6$ (ohm^{-1} $cm.^{-1}$).

Temp.	P (atm.)	1	1000	2000	3000
25°		1·5	2·1	2·7	3·0
45		3·2	5·0	5·9	6·5
65		5·1	7·4	9·3	11·5

[10] Dorsey, " Properties of Ordinary Water-substance," Amer. Chem. Soc. Monograph No. 81, 1940.

TABLE 6. *"Carbonic acid."*

100 × concn. (molal)	P (atm.)	$\Lambda\rho_r$	$\Lambda^1\rho_r$	$\gamma_\pm^2$	K_a^P/K_a^1 * (molal scale)
		At 25°			
2·56	1	1·606	394	0·977	(4·2 × 10^{-7})
,,	2080	5·332	454	0·966	8·26
,,	2930	7·821	468	0·961	16·7
2·91	1	1·528	394	0·974	(4·3 × 10^{-7})
,,	1050	2·918	430	0·969	3·04
,,	2040	4·945	454	0·963	7·85
,,	2930	7·455	468	0·958	16·7
2·92	1	1·493	394	0·974	(4·1 × 10^{-7})
,,	1270	3·243	435	0·969	3·85
,,	2540	6·147	463	0·960	12·2
2·73	1	1·538	394	0·976	(4·1 × 10^{-7})
,,	1050	2·951	431	0·972	3·07
,,	2070	5·071	455	0·969	8·14
,,	2860	7·532	468	0·960	16·9
2·05	1	1·777	394	0·979	(4·1 × 10^{-7})
,,	1030	3·353	430	0·975	2·98
,,	2010	5·725	454	0·970	7·81
,,	2930	8·743	469	0·963	17·0
3·20	1	1·402	394	0·976	(4·0 × 10^{-7})
,,	1010	2·606	439	0·972	2·90
,,	2010	4·458	454	0·963	7·54
,,	2850	6·873	467	0·959	16·9
$\Delta V^1 = -26·5$ c.c. mole^{-1}; $\Delta V^{3000} = -20·7$ c.c. mole^{-1}; Average $\Delta K = -0·0019$ atm.$^{-1}$ c.c. mole^{-1}.					
		At 35°			
3·32	1	1·696	448	0·974	(4·7 × 10^{-7})
,,	1390	3·809	492	0·966	4·16
,,	2930	7·791	521	0·956	15·5
3·19	1	1·714	448	0·974	(4·6 × 10^{-7})
,,	1030	3·161	481	0·969	2·93
,,	2040	5·343	507	0·962	7·54
,,	2930	7·968	521	0·956	15·9
3·46	1	1·695	448	0·974	(4·9 × 10^{-7})
,,	1010	3·066	481	0·968	2·82
,,	2040	5·261	507	0·961	7·46
,,	2930	7·856	521	0·955	15·8
1·51	1	2·558	448	0·978	(4·9 × 10^{-7})
,,	1030	4·720	482	0·973	2·94
,,	2030	7·940	507	0·968	7·51
,,	2930	11·85	521	0·963	15·9
1·18	1	2·970	448	0·979	(5·1 × 10^{-7})
,,	1390	6·386	492	0·974	3·83
,,	2640	12·01	517	0·966	12·3
2·53	1	1·972	448	0·977	(4·8 × 10^{-7})
,,	1390	4·397	492	0·970	4·11
,,	2780	8·527	519	0·961	13·9
3·40	1	1·674	448	0·975	(4·7 × 10^{-7})
,,	1050	3·130	482	0·970	3·00
,,	2030	5·144	507	0·964	7·33
,,	2930	7·700	521	0·959	15·6
$\Delta V^1 = -25·4$ c.c. mole^{-1}; $\Delta V^{3000} = -20·0$ c.c. mole^{-1}; Average $\Delta K = -0·0018$ atm.$^{-1}$ c.c. mole^{-1}.					
		At 45°			
2·99	1	2·066	506	0·976	(4·9 × 10^{-7})
,,	1320	4·250	547	0·968	3·61
,,	2500	7·397	576	0·960	9·83
2·48	1	2·276	506	0·975	(4·9 × 10^{-7})
,,	1030	4·117	540	0·970	2·85
,,	2010	6·728	565	0·965	6·99
,,	2930	10·11	586	0·960	14·7
3·74	1	1·903	506	0·972	(5·2 × 10^{-7})
,,	1030	3·420	540	0·967	2·83
,,	2030	5·614	565	0·961	6·95
,,	3000	8·544	587	0·954	14·9

* Values of K_a at $P = 1$ in parentheses.

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TABLE 6. (*Continued.*)

100 × concn. (molal)	P (atm.)	Λ_{ρ_T}	$\Lambda^1_{\rho_T}$	$\gamma_\pm^2$	K_a^P/K_a^1 * (molal scale)
		At 45°			
3·71	1	1·850	506	0·972	(4·8 × 10⁻⁷)
,,	1010	3·238	539	0·968	2·70
,,	2010	5·328	565	0·962	6·63
,,	2780	7·487	582	0·957	12·3
,,	2930	7·933	585	0·956	13·7
2·94	1	2·075	506	0·976	(4·8 × 10⁻⁷)
,,	1020	3·633	539	0·970	2·70
,,	2010	5·951	565	0·964	6·57
,,	3000	9·192	587	0·959	14·5
2·48	1	2·264	506	0·975	(4·9 × 10⁻⁷)
,,	1390	4·931	549	0·969	4·03
,,	2780	9·30	583	0·961	12·7
,,	3000	10·16	588	0·959	14·9
$\Delta V^1 = -24·8$ c.c. mole^{-1}; $\Delta V^{3000} = -18·4$ c.c. mole^{-1}; Average $\Delta K = -0·0021$ atm.$^{-1}$ c.c. mole^{-1}.					
		At 55°			
3·71	1	2·009	550	0·973	(4·8 × 10⁻⁷)
,,	1350	4·195	595	0·963	3·70
,,	2850	7·996	632	0·958	11·9
2·50	1	2·544	550	0·974	(5·2 × 10⁻⁷)
,,	1020	4·444	584	0·970	2·71
,,	2010	7·159	613	0·965	6·37
,,	2780	9·932	631	0·961	11·6
2·37	1	2·549	550	0·974	(5·0 × 10⁻⁷)
,,	1740	6·291	606	0·967	5·01
,,	2850	10·15	631	0·961	12·05
2·49	1	2·443	550	0·974	(4·8 × 10⁻⁷)
,,	1020	4·295	585	0·970	2·73
,,	2440	8·252	622	0·963	8·90
,,	2840	9·740	632	0·960	12·0
,,	2940	10·12	634	0·960	12·9
1·45	1	3·297	550	0·978	(5·1 × 10⁻⁷)
,,	1020	5·865	586	0·972	2·79
,,	2010	9·373	613	0·970	6·52
,,	2810	13·11	631	0·965	12·0
,,	2930	13·70	634	0·964	13·1
3·37	1	2·116	550	0·973	(4·9 × 10⁻⁷)
,,	720	3·189	574	0·969	2·08
,,	1770	5·364	607	0·967	5·28
,,	3000	9·133	635	0·966	14·0
2·72	1	2·353	550	0·974	(4·9 × 10⁻⁷)
,,	1420	5·017	596	0·968	3·87
,,	2930	9·857	634	0·959	13·19
$\Delta V^1 = -24·3$ c.c. mole^{-1}; $\Delta V^{3000} = -17·5$ c.c. mole^{-1}; Average $\Delta K = -0·0023$ atm.$^{-1}$ c.c. mole^{-1}.					
		At 65°			
2·46	1	2·706	606	0·975	(4·8 × 10⁻⁷)
,,	1080	4·726	644	0·971	2·70
,,	2080	7·558	671	0·966	6·34
,,	2850	10·45	689	0·963	11·5
2·32	1	2·845	606	0·975	(5·0 × 10⁻⁷)
,,	1010	4·922	642	0·972	2·67
,,	2010	7·886	669	0·965	6·30
,,	2700	10·44	685	0·961	10·5
,,	2780	10·87	687	0·961	11·3
3·71	1	2·193	606	0·974	(4·8 × 10⁻⁷)
,,	1060	3·840	642	0·968	2·72
,,	2080	6·127	671	0·962	6·33
,,	2790	8·215	687	0·959	10·8
1·59	1	3·380	606	0·978	(4·9 × 10⁻⁷)
,,	1400	6·997	653	0·972	3·68
,,	2790	12·69	688	0·965	10·9
2·50	1	2·724	606	0·975	(5·0 × 10⁻⁷)
,,	1040	4·729	642	0·970	2·67
,,	2570	9·531	683	0·963	9·62
$\Delta V^1 = -23·6$ c.c. mole^{-1}; $\Delta V^{3000} = -16·8$ c.c. mole^{-1}; Average $\Delta K = -0·0023$ atm.$^{-1}$ c.c. mole^{-1}.					

* Values of K_a at $P = 1$ in parentheses.

Wherever possible, accurate values of Λ^1 from other measurements [11–13] are included with the conductance ratios in the Tables. The units of the Λ values reported are cm.^{2} ohm^{-1} mole^{-1}.

Table 6 gives the results for the changes with pressure of the apparent dissociation constant K_a of carbonic acid. The product $\Lambda\rho_T$ (and hence $\alpha = \Lambda\rho_T/\Lambda'\rho_T$) was obtained from the specific conductivities L' by the relation $\Lambda\rho_T = 1000L'/m\rho^1$, where ρ^1 is the density of the acid solution (~water) at 1 atm. pressure.

The volume change on ionisation at infinite dilution was calculated from the slope of log $(K_a{}^P/K_a{}^1)$ *versus* pressure graphs at 1 atm. (ΔV^1) and at 3000 atm. (ΔV^{3000}).

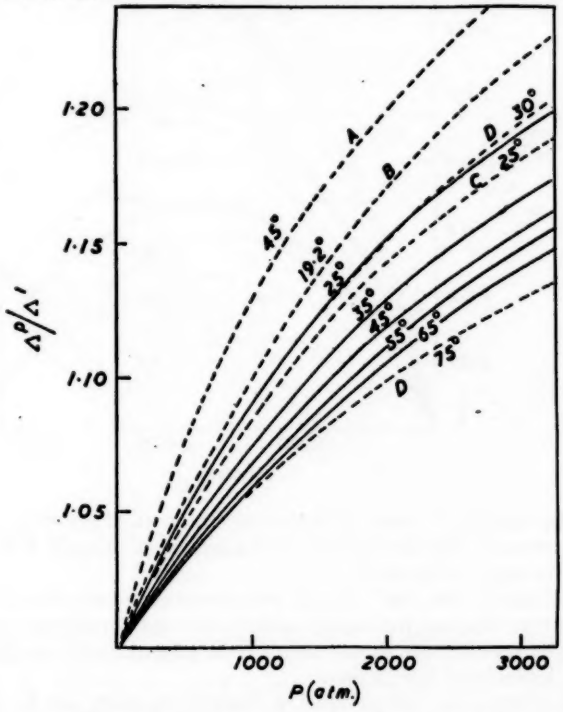
$$(\delta \ln K_a)/(\delta P)_{T,m} = -\Delta V/RT \qquad (-\delta\Delta V/\delta P)_{T,m} = \Delta K \approx (\Delta V^{3000} - \Delta V^1)/3000$$

From the latter relation the average value for the change in compressibility (ΔK) on ionisation in the pressure range 1—3000 atm. was obtained at each temperature.

Discussion

Figs. 1—3 summarise the results for hydrochloric acid, potassium chloride, and potassium hydrogen carbonate, and also show some values of $\Lambda^P\rho_T/\Lambda^1$ obtained by previous

Fig. 1. 0·01m-*Hydrochloric acid.* —— *Our values.* ---- *Literature values: A, Hamann and Strauss, ref.* 7; *B, Korber, ref.* 14; *C, Buchanan and Hamann, ref.* 9; *D, Zisman, ref.* 5.



workers. The agreement is not good, and the results of Hamann and Strauss [7] are anomalous. The effect of pressure on conductance was found to decrease with temperature in the manner reported by Korber [14] and Zisman.[5]

[11] Owen and Sweeton, *J. Amer. Chem. Soc.*, 1941, **63**, 2811.
[12] Gunning and Gordon, *J. Chem. Phys.*, 1942, **10**, 126.
[13] Shedlovsky and MacInnes, *J. Amer. Chem. Soc.*, 1935, **54**, 1429.
[14] Korber, *Z. phys. Chem.*, 1909, **67**, 212.

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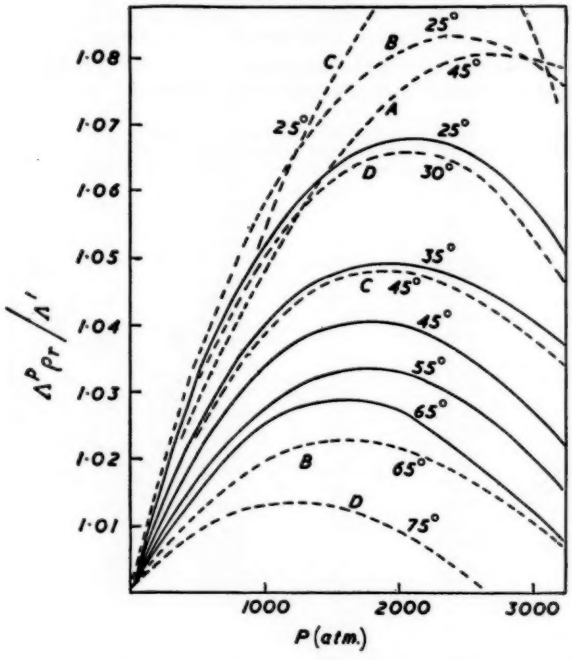
Zisman [5] and Hamann and Strauss [7] examined the effects of pressure on conductance up to pressures of 10,000 atm. The latter workers suggested that Zisman's results were in error by several units %, but the present observations do not support this suggestion.

Fig. 4 shows the ratios Λ_0^P/Λ_0^1 for potassium hydrogen carbonate solutions, together with Bridgman's ratios [15] of the viscosity η^1/η^P for 18°, 30°, and 75°. The variation of Λ_0^P/Λ_0^1 with pressure is similar for most salts in that the values pass through an initial maximum or a curvature in the same sense before decreasing steadily with increasing pressure.

For 16 salts Zisman [5] showed that at 30° and 75° the ratio Λ^P/Λ^1 decreased almost linearly with pressure in the range 3000—8000 atm., and always with the same slope.

FIG. 2. 0·01m-*Potassium chloride.*



The increase in the viscosity of water at these temperatures and pressures is also approximately linear with pressure, but the increase in viscosity is more rapid than the decrease in conductance for the same temperature.

The compressibility of ions, derived from measurements on crystals of the alkali halide type, is only about one tenth of the compressibility of water at moderate pressures.[15] The effect of pressure on conductance should therefore be related mainly to changes in solvent structure and in ion–solvent interaction.

For a 1 : 1 electrolyte the Debye–Hückel–Onsager equation can be written [16] in the form

$$\Lambda_0 - \Lambda = \left[\frac{A\Lambda_0}{(DT)^{3/2}} + \frac{B}{\eta(DT)^{1/2}}\right]c^{1/2}$$

A and B are positive constants and D is the dielectric constant.

[15] Bridgman, " The Physics of High Pressures," G. Bell and Sons, London, 1931.
[16] MacInnes, " The Principles of Electrochemistry," Reinhold, New York, 1939.

Both D and η for pure water increase at high pressures and Λ_0 decreases. As discussed by Hamann,[3] the effect of pressure on conductance could be expected to decrease with increasing concentration. For example, for potassium chloride it would be expected that at 3000 atm. Λ_0^P/Λ_0^1 would be about 3·5% greater than Λ^P/Λ^1 for a 0·1M-solution.

Variations with concentration of this order were not found in the present experiments with solutions up to 0·1M. However, Korber's results [14] provide a good example of the decreasing pressure effect at higher concentrations.

The apparent disagreement with the Debye–Hückel–Onsager equation below 0·1M must result from the assumption that the values of D and η for the salt solutions at high

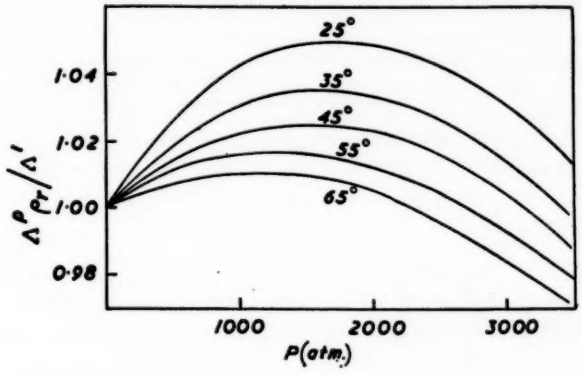


FIG. 3. 0·01m-*Potassium hydrogen carbonate.*

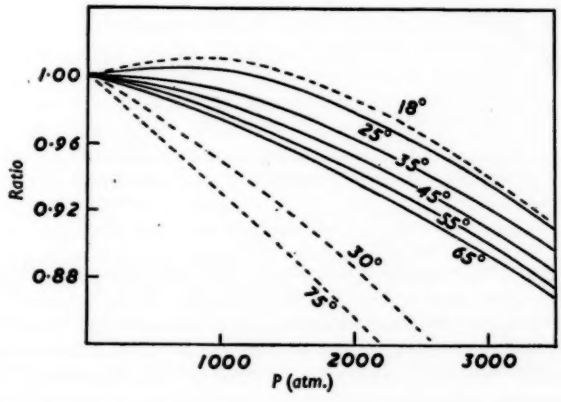


FIG. 4.

——— *Values of* Λ_0^P/Λ_0^1 *for* $KHCO_3$ *solutions at* 25°, 35°, 45°, 55°, *and* 65°.

– – – – *Bridgman's values for ratio* η^1/η^P *at* 18°, 30°, *and* 75°

pressures correspond to those for water at the same temperature. Zisman [5] showed that the initial maximum in the graph of Λ^P/Λ^1 for neutral salts was greatest and occurred at highest pressures for small ions of high valency. These are order-producing ions which, in the terminology of Frank and Evans,[17] lower the structural temperature of water. In Fig. 4 the variation of η^1/η^P with pressure corresponds to the ratio Λ_0^P/Λ_0^1 for a rather higher temperature. It is not sufficient to relate the changes in conduction at high pressure with the changes in physical properties of pure water at the same temperature.

For aqueous solutions there appear to be two opposing factors in operation which tend to counterbalance each other with changing concentrations below about 0·1M. The

[17] Frank and Evans, *J. Chem. Phys.*, 1945, **13**, 507.

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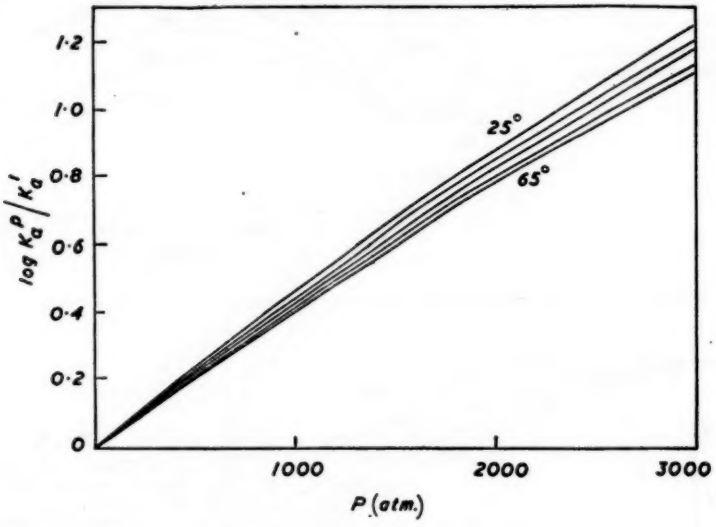
decreased pressure effect on conductance predicted at higher concentrations by the Debye–Hückel–Onsager relationship is opposed by the lower structural temperature of water at increased salt concentrations. The pressure effect on conductance in water is greatest at low temperatures.

For " carbonic acid," ΔV^1 becomes more positive with increasing temperature. A similar behaviour was calculated by Owen and Brinkley [18] for ΔV^1 for the ionisation of water. They considered that ΔV^1 would continue to increase with temperature until at very high temperatures the ionisation of weak acids was decreased by pressure. It is thought more likely that ΔV^1 increases with temperature, passes through a maximum, and becomes increasingly negative at high temperatures. The present results for " carbonic acid " show that the increase in ΔV^1 for a given temperature rise becomes less at higher

FIG. 5. *The variation with pressure of the apparent dissociation constant of " carbonic acid " in the temperature range* 25—65°.



temperatures. It is known that at temperatures approaching, and exceeding the critical temperature of water, increased pressure greatly increases the ionisation of all electrolytes.[19]

The effect of pressure on the ionisation of " carbonic acid " has not been studied before in detail, although Brander [20] found that pressure had an abnormally large influence on the conductance of carbon dioxide solutions. Owen and Brinkley [18] calculated ΔV^1 at infinite dilution by use of experimental values for the partial molal volumes of the hydrogen and bicarbonate ions, and of carbon dioxide in solution.

Owen and Brinkley's estimated value of ΔV^1 for "carbonic acid " at 25° was −29 c.c. mole^{-1}, but it was based on an early experimental value of the partial molar volume of carbon dioxide in solution. They assumed that $-\Delta K$ for ionisation was greater than $1{\cdot}0 \times 10^{-3}$; the present results show it to be equal to $1{\cdot}9 \times 10^{-3}$ at 25°.

True carbonic acid, H_2CO_3, has a dissociation constant at 25° and 1 atm. of $1{\cdot}72 \times 10^{-4}$, which is very close to the value of K_a given by Harned and Owen [21] for formic acid ($1{\cdot}772 \times$

[18] Owen and Brinkley, *Chem. Rev.*, 1941, **29**, 461.
[19] Ellis and Fyfe, *Rev. Pure and Appl. Chem.*, 1957, **7**, 261.
[20] Brander, *Soc. Sci. Fenn., Phys. Math.*, 1932, **6**, 1.
[21] Harned and Owen, " The Physical Chemistry of Electrolyte Solutions," Reinhold, New York, 1950.

10^{-4} at 25°). As the two molecules are very similar they would be expected to differ only slightly in properties:

If it is assumed that ΔV^1 at 25° for the ionisation of H_2CO_3 is equal to that for formic acid (−8·8 c.c. mole^{-1}),[7] a value of ΔV_h for the hydration of carbon dioxide to carbonic acid can be obtained:

$$\Delta V_h \approx \Delta V^1 \text{ (" carbonic acid ")} - \Delta V^1 \text{ (formic acid)} = -17{\cdot}7 \text{ c.c. mole}^{-1}.$$

It is evident that pressure has a considerable influence on the hydration of carbon dioxide, and it would be expected to have a similar effect on the hydration of other gases which form ionised solutions, *e.g.*, ammonia, amines, sulphur dioxide. In a 0·1M-ammonia solution, Moore and Winmill [22] found that NH_3 was present to the extent of 46·2% and $NH_4{\cdot}OH$ 52·4%. The true dissociation constant of $NH_4{\cdot}OH$ is about 4×10^{-5}.

Hamann [3] considered that the increased ionisation of weak electrolytes at high pressure was due essentially to the enhanced solvation of the ions with respect to the un-ionised molecules. He calculated the change in free energy of hydration of singly charged ions at high pressures using Born's formula:

$$\Delta G^\circ \text{ (solvation)} = -\frac{Ne^2}{2r}\left(1 - \frac{1}{D}\right)$$

where N is Avogadro's number, e the electronic charge, D the dielectric constant, and r the mean radius of the two ions. As r decreases and D increases with pressure, ΔG° (solvation) increases.

That this is an oversimplification for weak acids and bases of the hydrated gas type is shown by the present series of results. A calculation for the effect of pressure on ammonia ionisation was given by Hamann,[3] using the compressibility of cæsium fluoride as a model for the compressibilities of the ammonium and hydroxyl ions. The values obtained for the ratio K_a^P/K_a^1 were lower than those from experiment by a factor of about two over the pressure range 3000—6000 atm. This would indicate that ammonia is present in solution at these pressures almost entirely as $NH_4{\cdot}OH$.

If ΔV_h is assumed not to change appreciably with pressure at 25°, the fraction of carbon dioxide in solution present as H_2CO_3 rises from 0·259% at 1 atm. to 2·3% at 3000 atm.

It is evident therefore that the Born equation should not be used to predict the increase with pressure in the apparent ionisation constant for substances such as CO_2, SO_2, and NH_3, where a hydration step precedes ionisation.

This work was done at the Chemistry Department, University of Otago, and the author thanks Prof. H. N. Parton and Dr. W. S. Fyfe for their helpful comments. He also thanks the Director, Dominion Laboratory, for permission to publish.

Dominion Laboratory, Department of Scientific and Industrial Research,
Wellington, New Zealand. [*Received, January 16th*, 1959.]

[22] Moore and Winmill, *J.*, 1912, **101**, 1635.

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751. *Factors influencing the Rates of Dissociation of Metal Complexes. Part I. The Mechanism of Dissociation of Mono(ethylenediamine)-nickel(II) Ion.**

By A. K. Shamsuddin Ahmed and R. G. Wilkins.

The rate of dissociation of $[Ni\ en(H_2O)_4]^{2+}$ into nickel ion and ligand has been examined in aqueous solution at 0° over a wide range of pH. The rate increases about twenty-fold from pH 7·3 to 4, then remains constant until pH 1·5, and increases again at higher acid concentration. These rates are estimated from (*a*) $^{63}Ni^{2+}$ exchange experiments (in the pH region where no net chemical reaction occurs), (*b*) the rate of consumption of acid added to maintain constant pH as amine is liberated from the dissociating complex (pH 5 to 2), and (*c*) spectrophotometry (at acidities greater than 0·01M).

The complex acid-dependence can be explained in terms of a rate-determining step (rate constant k_2) involving the first bond rupture of the bidentate ligand measured by the constant rate in weakly acid solution. A comparison of $^{63}Ni^{2+}$ and ^3H_2O exchange studies with the complex, at chemical equilibrium, in neutral solution also yields a value for k_2 and the agreement from the independent approaches is good. The enhanced rate in highly acid solution results from proton-aided rupture of the first bond, the contribution being directly proportional to C_{H^+}. In a dilute solution of $[Ni\ en(H_2O)_4]^{2+}$ in 2M-perchlorate, $k_2 = 10^{16} \exp(-20{,}500/RT)$ min.$^{-1}$. The significance of the results is discussed.

Although there is considerable information about the successive stability constants for many organic chelate systems [1] there are, unfortunately, many fewer data on the formation and dissociation † rates of metal complexes and of the many factors influencing these rates. Further, the study of the mechanism of dissociation of simple chelates has not led to completely satisfactory results.[2a] In an attempt to remedy some of these deficiencies, the present work was commenced.

Our earlier studies of ethylenediamine exchange and acid dissociation of $[Ni\ en_3]^{2+}$ in water,[3] as well as the dissociation studies in methanol at low temperatures,[4] indicated that the dissociation of $[Ni\ en]^{2+}$ should be measurable at 0°. The mono-complex is the simplest to investigate and interpret, since we are not concerned then with multiple ligand dissociation. The rate behaviour over a wide range of pH should give insight into the detailed mechanism of chelate dissociation and if, in addition, we study the exchange of amine hydrogen with water using the now readily available tritium (^3H) isotope we might differentiate any stages of co-ordinated and free amine groups during the stepwise dissociation. We were encouraged in the latter respect by the work of Carter, Odell, and Llewellyn,[2b] who showed from $H_2{}^{18}O$ exchange that one oxalate group of $[Cr(oxal)_3]^{3-}$ must open and close at one end many times before complete rupture, although the quantitative interpretation of their results was complicated.

Experimental

Materials.—Nickel perchlorate solutions were obtained by dissolving well-washed freshly precipitated nickel hydroxide (obtained from " AnalaR " nickel nitrate and sodium hydroxide)

* Presented in part at the International Conference on Co-ordination Chemistry, London, April 1959.

† The terms aquation and hydrolysis have also been used with the same connotation.

[1] " Stability Constants," Part I, Organic Ligands, The Chemical Society, London, 1957.

[2] Basolo and Pearson, " Mechanisms of Inorganic Reactions," Wiley, New York, 1958, (*a*) p. 152 *et seq.*, (*b*) p. 272.

[3] Popplewell and Wilkins, *J.*, 1955, 4098.

[4] Bjerrum, Poulsen, and Poulsen, " Proceedings of the Symposium on Co-ordination Chemistry " Danish Chemical Society, 1954, p. 51.

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in the minimum of " AnalaR " perchloric acid. The solution was standardised by complexometric analysis.[5] Ethylenediamine nitrate and perchlorate were prepared from distilled ethylenediamine. $^{63}Ni(NO_3)_2$ solution was obtained as described previously,[6] and tritiated water purchased from A.E.R.E., Harwell. The following nickel complexes were prepared:

$[Ni\ en(H_2O)_4](NO_3)_2$. Nickel nitrate hexahydrate (15 g.) was dissolved in water (5 c.c.). and ethylenediamine hydrate (1 g.) added. The warm solution was cooled in ice, and the pale blue crystals of the *mono-complex* were filtered off, washed with a small amount of ice-cold water, then acetone, and finally air-dried (yield 3·0 g.) (Found: C, 7·45; H, 5·05; Ni, 18·8; H_2O, 23·2. $C_2H_{16}N_4NiO_{10}$ requires C, 7·6; H, 5·1; Ni, 18·7; H_2O, 22·9%). The tritium-labelled compound was prepared on about 1/5th of this scale by using ethylendiamine hydrate in ^3H_2O.

$[Ni\ en(H_2O)_4][C_{10}H_6(SO_3)_2],2H_2O$.[7] This was precipitated when a saturated solution of disodium naphthalene-1,5-disulphonate was added to a solution containing the $[Ni\ en]^{2+}$ ion (Found: en, 11·6; Ni, 11·4; H_2O, 21·6. Calc. for $C_{12}H_{26}O_{12}N_2S_2Ni$: en, 11·7; Ni, 11·5; H_2O, 21·1%). The substance turns green when heated at 60° over phosphoric oxide for several hours.[7]

Exchange Runs.—(a) *Nickel exchange.* The separation of $[Ni\ en]^{2+}$ from Ni^{2+} proved difficult. Many anions were tried but the only satisfactory one proved to be naphthalene-1,5-disulphonate, which precipitated the complex, free from nickel ion, when the concentration of the former exceeded 0·04M. Nickel ion (0·12—0·20M) and ethylenediamine salt (0·04—0·08M) were mixed, pH was adjusted, neutral salt added, if required, and the solution settled to thermal equilibrium. Exchange was initiated by adding $^{63}Ni^{2+}$. At various times exchange was

TABLE 1. *Dissociation of* $[Ni\ en]^{2+}$ *to nickel ions in nitrate medium.*

Run no.	pH	[complex] (mmole l.$^{-1}$)	[nickel] (mmole l.$^{-1}$)	$t_{\frac{1}{2}}$ (min.)	10^3R Ni (min.$^{-1}$ mole l.$^{-1}$)	10^3k_{Ni} (min.$^{-1}$)
		(*a*) pH range 7·3—5·7 ($^{63}Ni^{2+}$ exchange studies) at 0·2°				
1	7·3	80·0	120·0	10·0	3·3	4·15
2	7·1	80·0	120·0	8·5	3·9	4·9
3	6·8	80·0	120·0	4·9	6·8	8·5
4[a]	6·8	80·0	120·0	4·8	6·9	8·6
5[a]	6·8	80·0	200·0	5·7	7·0	8·75
6[a]	6·8	40·0	120·0	6·3	3·3	8·25
7[b]	6·8	40·0	120·0	6·1	3·4	8·5
8	6·2	69·0	131·0	4·0	7·5	11·3
9	5·7	54·7	145·3	2·1	10·5	23·7
		(*b*) pH range 5·0—2·1 (H^+ consumption) at 0·2°.				
10	4·9	80·0	200·0	1·28	—	54
11	4·0	80·0	200·0	1·08	—	64
12	3·0	100·0	200·0	1·03	—	67
13	2·1	80·0	120·0	1·03	—	67
		(*c*) pH 1·0 (spectral) at 0·6°.				
14	1·0	100·0	200·0	1·00	—	69
		(*d*) ^3H_2O exchange studies at 0·6°.				
					10^3R_H	10^3k_2
15	7·1	100·0	200·0	1·75	158	74
16	6·7	153·0	200·0	1·43	297	88
17[c]	6·7	80·0	200·0	1·53	145	82
18	6·2	80·0	200·0	1·50	148	81
19	1·5	80·0[d]	200·0	<5% in 1 min.		—

[a] Ionic strength = 1·0M-nitrate. [b] Ionic strength = 2·0M, in perchlorate medium. [c] ^3H_2O being used. [d] Complex concentration at commencement of run.

quenched by adding an ice-cold saturated solution of disodium naphthalene-1,5-disulphonate to the mixture, shaking vigorously, and then scratching hard with a sharp glass rod. A blue precipitate of the mono-complex, $[Ni\ en(H_2O)_4][C_{10}H_6(SO_3)_2],2H_2O$, appeared, usually within

[5] Schwarzenbach, " Complexometric Titrations," transl. by Irving, Methuen, London, 1957.
[6] Wilkins and Williams, *J.*, 1957, 4514.
[7] Pfeiffer, Dominik, Fritzen, and Werdelmann, *Z. anorg. Chem.*, 1949, **260**, 84.

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10—20 sec., otherwise the point was abandoned, and the point of " clouding " was taken as the exchange time. The precipitate was quickly centrifuged, washed twice with cold water, and dissolved in dilute hydrochloric acid, and nickel was precipitated with dimethylglyoxime and ammonia. ^{63}Ni assay was as described previously.[6] Only a very small " zero-time " exchange was obtained by this procedure (Fig. 1, Curve *A*). The results are in Table 1(*a*). Spectral analysis of Run 3 showed that the mono-species predominated with maxima at 372, 625, and 980 mμ (Ballhausen [8a] reports 370, 640, and 980 mμ), and inflection point at *ca.* 730 mμ.[8b] This was verified from the known stability data.[1] Runs 3—7 indicated that Rate = k_{Ni}[complex], even though it was strongly pH-dependent, and that at pH = 6·8 the value of k_{Ni} did not vary in 0·76M and 1·0M-nitrate and 2.0M-perchlorate. The rate data are not accurate for Runs 8 and 9 because of relatively large zero-time exchange. This arises from complex dissociation (*ca.* 15 and 30% respectively from spectral data) at these pH.

(b) *Hydrogen exchange.* Basically the method was similar to (a). The equilibrium of [Ni en]$^{2+}$ and Ni^{2+} was set up and exchange initiated by the addition of the tritiated nickel complex. The separated complex naphthalenedisulphonate was washed with cold water (no heterogeneous exchange occurs at this stage), then alcohol and ether, air-dried, and radio-assayed as described below. In one run (No. 17) $^1H^3HO$ was added to the exchange mixture, and the increase in activity of the precipitated complex measured. This will not start from zero because of the presence of tritiated water in the solid. It is necessary in this case to use the precipitant in $^1H^3HO$ of similar specific activity to that in the exchange mixture, this being much easier than mixing known volumes, accurately, of reactants and precipitants at these temperatures and exchange speeds. In order to follow an exchange completely the following detailed procedure was adopted in one run (No. 16) with the experimental results shown (see also Fig. 1, Curve *B*): [Ni *en(*H_2O)$_4$](NO$_3$)$_2$, prepared as described earlier, and naphthalenedisulphonate added to filtrate gave [Ni *en(*H_2O)$_4$] naphthalenedisulphonate,2*H_2O, which gave 3460 counts/min. Therefore [Ni *en(*H_2O)$_4$] naphthalenedisulphonate,2H_2O gives 2595 counts/min. Then [Ni *en(*H_2O)$_4$](NO$_3$)$_2$ (30 mg.) was added to Ni^{2+} (1·0 c.c., 0·2M, pH ~6) and the complex was precipitated with saturated naphthalenedisulphonate solution (1·0 c.c.), all solutions being pre-cooled to 0°. This procedure was repeated for each exchange point and at the end of the exchange. The value at zero time was 837 counts/min. Thus all the hydrogen in the water of [Ni *en(*H_2O)$_4$](NO$_2$)$_2$ has exchanged immediately (1/3 × 2595 = 865). The remaining slower process with only a small zero-time exchange is due to exchange of amine-hydrogen, the final equilibrium value being 37 counts/min. It is difficult to calculate an equilibrium value since there will almost certainly be an isotope effect and the precipitated complex contains both types of hydrogen, amine, and water and the specific activites of these will differ.

There being no isotope effect on the rate R_H (see below), $R_H = (0{\cdot}693/t_{\frac{1}{2}}) \times 4$[complex]. In both nickel and hydrogen exchanges reasonably good first-order exchange plots were obtained (Fig. 1).

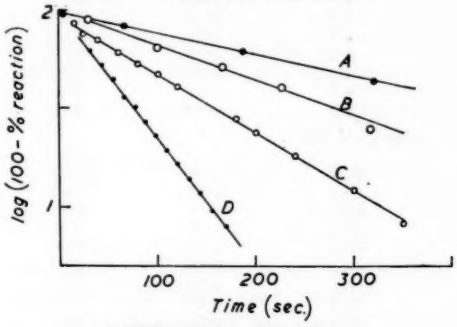
(c) *Tritium assay.* All measurements were made with dry samples, in a Packard (U.S.A.) gas-flow proportional counter, methane or (less satisfactorily) argon–methane being used. The solid was spread over a cylindrical depression in a thick aluminium disc and firmly " matted " by steady pressure at the end of a cylindrical rod placed over the sample.[3] It was found unnecessary to incorporate graphite in the sample [9] to obtain reproducibility in count rate. " Infinite thickness " is easily reached with 0·6 mg. cm.$^{-2}$ or more.[10] The important quantity in exchange reactions is relative specific activity, and this is measured by relative count rates, since the other factors which affect the latter (geometry, back-scattering, etc.) are constant. The same amount, approximately, of material ($\geqslant$0·6 mg. cm.$^{-2}$) was used in each sample since the count rate was a little sensitive to sample height. Reproducibility of counting was about ±5%. The background varied from 20 to 30 counts/min.

H$^+$-*Consumption Experiments.*—As the complex dissociates, the free amine liberated increases the pH value. Constant pH can be maintained by controlled addition of acid, the rate of which measures d[Ni en^{2+}]/d*t*. In early experiments we used a Radiometer titrator (Copenhagen), acid being added from a micro-syringe by means of an electronic relay, and the rate

[8] (*a*) Ballhausen, *Dansk. Mat. Fys. Medd.*, 1955, **29**, No. 8; (*b*) Jörgensen, *Acta Chem. Scand.*, 1956, **10**, 887.
[9] Banks, Crawhall, and Smyth, *Biochem. J.*, 1956, **64**, 411.
[10] Rydberg, *Acta Chem. Scand.*, 1958, **12**, 399.

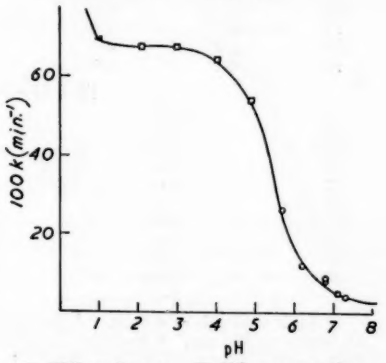
of acid consumption recorded automatically.[11] Although this arrangement was convenient we found that the apparatus did not always respond quickly to pH changes because of the relatively fast dissociation rates studied in this and similar work. We therefore replaced the automatic features by a manual Morse key which operated a solenoid valve attached to the burette. With the key in the " on " position the burette valve was opened and a small controlled volume of acid was admitted to the well-stirred reaction solution, the tip of the burette extended to a fine jet being below the surface of the solution. With this arrangement there was no difficulty in holding the pH within 0·05 unit as the dissociation proceeded or in observing the burette reading, so that half-lives as short as 30 sec. could be accurately measured. In the runs at higher concentrations of reactants for comparison with the exchange runs [Table 1(*b*)] about 15 c.c. of solution were used and 1M-nitric acid as added acid. In the perchlorate runs [Table 2(*a*)], 2M-sodium perchlorate (75—100 c.c.) at the required pH was cooled to 0°, a pre-cooled solution of the complex (2 c.c. of 0·1M-complex, 0·2M-nickel, at pH 6·8) rapidly

FIG. 1. *Typical first-order curves.*



A, ^{63}Ni exchange (Run 4).
B, ^{3}H exchange (Run 16).
C, H^+-consumption (Run 24).
D, Spectral (Run 38).
The time-ordinate is doubled for *B*.

FIG. 2. *Variation of first-order rate constant for* $[Ni\ en]^{2+} \longrightarrow Ni^{2+}$ *change with* pH. $[Ni\ en^{2+}] = 40—80$ mM, $[Ni^{2+}] = 120—200$ mM, $\mu = 0·8—1·0$M-NO_3^-.



○ ^{63}Ni exchange. □ H^+-consumption. △ Spectral.

added, and the rate of addition of acid (0·1 or 1·0M-perchloric acid in 2M-perchlorate) recorded as the pH was maintained constant. A typical experimental curve is shown in Fig. 1, Curve *C*, which shows a slight initial curvature observed in some runs owing to the presence of a small amount of the bis-species ($t_{\frac{1}{2}} \sim 5$ sec.) which dissociates more rapidly than the mono-species. The consumption of acid corresponded to that calculated for two amine groups. Runs 20, 21, 23 (with 31) show that the rate constant is independent of the concentrations of complex, products, and perchlorate.

Spectrophotometry.—The spectra of $[Ni\ en]^{2+}$ and Ni^{2+} (cf. ref. 8) show their greatest absorption difference around 900 mμ, and we used this wavelength to follow the change. In one case, we found an identical rate when we used instead 550 mμ. At 422 mμ, an isosbestic point, no absorption change occurred during the dissociation. Because of the rapid dissociation in excess of acid, it was necessary to study the reaction at ice-water temperature. A Perspex container was constructed which could fit, in a reproducible position, into the cell compartment of a Unicam SP.600 spectrophotometer. The container was divided into a central portion which contained the reaction solution and interrupted the light path (45 mm.) of the spectrophotometer. This central portion was surrounded by ice-water on both sides as well as underneath. A Perspex lid fitted tightly over the container. " Misting " on the cell face was avoided by passing cold dry air through the spectrophotometer compartment for about 1 hr.

[11] For a discussion see Jacobsen, Leonis, Linderstrøm-Lang, and Otteson, in " Methods of Biochemical Analysis," ed. Glick, Interscience, New York, 1954, Vol. 4, pp. 171 *et seq.* This method has been used extensively in biochemistry, but this work is apparently one of the first applications to complex ion kinetics.

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before, as well as during, the run. The procedure for a measurement was as follows: (i) Pre-cooled distilled water (*ca.* 15 c.c.) was placed in the central portion of the Perspex cell and optical balance obtained in " check " position. (ii) The water was removed and replaced by the reaction solution (10 c.c., *ca.* 0·02M-complex, 0·04M-nickel, ionic strength 2·0M-perchlorate) pre-cooled to 0·3°. Pre-cooled perchloric acid (with added sodium perchlorate, ionic strength 2·0M) was added (5 c.c.) and the cell and compartment lids were quickly replaced. " Misting " cleared within 15 sec. and optical densities could be read within 20 sec. of mixing.

TABLE 2. *Dissociation of* [Ni en]$^{2+}$ *to nickel ions in perchlorate medium of ionic strength* = 2·0M.

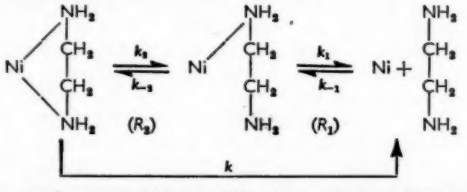
Run no.	Temp.	pH	[complex] (mmole l.$^{-1}$)	[nickel] (mmole l.$^{-1}$)	$t_{\frac{1}{2}}$ (min.)	10^2k_2 (min.$^{-1}$)
		(*a*) pH range 5·6—3·5 (H^+ consumption).				
20 [a]	0·2	5·5	0·8	2·0	1·80	38·5
21	0·3	5·4	3·3	5·0	1·82	38·1
22	0·3	5·2	2·6	3·9	1·75	39·6
23 [b]	0·3	4·0	3·3	—	1·68	41·2
24	0·3	3·5	2·6	3·9	1·75	39·6
25	2·25	4·0	2·9	4·3	1·35	51·4
26	2·25	4·0	2·9	4·3	1·33	52·1
27	4·3	4·0	2·9	4·3	1·03	67·3
28	4·3	4·0	2·9	4·3	1·03	67·3
29	6·1	4·0	2·9	4·3	0·82	84·5
		(*b*) 0·05—3·0M-$HClO_4$ (spectral, 0·6°).				
		[acid]				
30		0·03	13·3	20·0	1·85	37·5
31 [c]		0·10	100	200	1·67	41·5
32		0·33	26·7	40·0	1·52	45·7
33		0·68	26·6	40·0	1·23	56·3
34		1·08	26·7	40·0	1·07	65·0
35 [b]		1·50	30·0	—	0·88	78·7
36 [b]		1·50	30·0	—	1·05	66·0
37		1·58	26·7	40·0	0·90	77·0
38 [d]		2·08	26·7	40·0	0·77	90·3
39 [e]		3·15	26·7	40·0	0·67	104·0

[a] Ionic strength = 8·4mM. [b] [Ni en $(H_2O)_4$]$(NO_3)_2$ being used. [c] Reaction followed at 550 mμ; all others at 900 mμ. [d] Reaction in 85% D_2O. [e] Ionic strength >2·0M.

With this arrangement it was not easy to reach temperatures below 0·6° but the temperature stability was good, rising by less than 0·1° in 30 min. The optical density at the completion of the reaction was always small. After 30 min. the " check " with water still balanced. The linearity of the first-order plots over four or five half-lives is shown in Fig. 1, Curve *D*. Results were reproducible. Runs 14 and 31 show that with the concentration of complex at or above 0·1M, perchlorate has less accelerating effect than a nitrate (or chloride) medium.

DISCUSSION

Fig. 2 shows the variation with pH of the rate constant for *overall* dissociation (k) of [Ni en]$^{2+}$. The equilibria involved in this process can be represented as shown (co-ordinated water and charges have been omitted for convenience):



We shall refer to the species containing unidentate ethylenediamine as the intermediate in the subsequent discussion. In neutral solution and in acid solution, the equilibrium will lie to the left and to the right respectively. It is convenient to discuss the dissociative behaviour in terms of three regions.

Neutral Region.—The nickel-exchange rate (R_{Ni}) is markedly pH-dependent. This result can be understood from the above scheme. With the system at chemical equilibrium [12,13]

$$R_{Ni} = R_2R_1/(R_2 + R_1) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

If we denote the concentration of $[Ni\ en]^{2+}$ by a and that of the intermediate by b then

$$R_{Ni} = \frac{(k_2a)(k_1b)}{k_2a + k_1b}$$

and since

$$k_{-2}b = k_2a,\ R_{Ni} = \frac{k_2k_1a}{k_{-2} + k_1} = k_{Ni}a$$

This agrees with the observed first-order dependence on complex and lack of dependence on nickel-ion concentrations. Further there is also present, in amounts dependent on pH, a protonated form of the intermediate which will disrupt completely with its characteristic rate constant, but which is assumed to ring-close very lowly. This situation can be accommodated by expressing k_1 in the form $k_1 = k_1^{\circ} + k_1^{H}[H^+]$. For reasons which we shall see k_2 can be assumed to be acid-independent in this pH region. Therefore

$$k_{Ni} = \frac{k_2(k_1^{\circ} + k_1^{H}[H^+]}{k_{-2} + k_1^{\circ} + k_1^{H}[H^+]} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

From this it can be easily shown that

$$\frac{1}{(k_2 - k_{Ni})} = \frac{k_{-2} + k_1^{\circ}}{k_2k_{-2}} + \frac{k_1^{H}[H^+]}{k_2k_{-2}}$$

The linear plot of $1/(k_2 - k_{Ni})$ against $[H^+]$ is shown in Fig. 3. The value of k_2 can be obtained as described below. Extrapolation to $[H^+] = 0$ gives $k_{Ni} = 0{\cdot}033$ min.$^{-1}$, indicated by the limiting rate in Fig. 2 and reached at pH = 8. The onset of base catalysis may occur at this stage. It is not possible to perform nickel exchange above pH 7·4.

A comparison of nickel and hydrogen exchange rates at the same pH proves very fruitful. We must first establish that with our conditions, no *direct* hydrogen exchange occurs between the co-ordinated amine and water, as has been observed with certain ammines of cobalt(III), palladium(II), and platinum(II).[14,15,16] Our evidence is this: (i) we observe a constant hydrogen-exchange rate over a ten-fold change in hydrogen-ion concentration, whereas we should expect the rate to be a function of pH on any direct mechanism, *i.e.*, inversely proportional to $[H^+]$ on the basis of formation through a metal amide: [14,15,16]

$$OH^- + -M(NH_3)^{x+} \rightleftharpoons -M(NH_2)^{(x-1)+} + H_2O$$

(ii) we have obtained different rates of hydrogen exchange for other amines (to be described in subsequent papers) the values for which can be easily accommodated into our scheme but which would not otherwise be easily understood.

We assume then that on bond rupture, as an $-NH_2$ group is freed, rapid exchange between this and water occurs. We have confirmed that there is rapid ligand–water exchange at these pH. Tritium exchange (R_H) therefore is analogous to ligand exchange for the system

$$MA_4 \overset{(R_2)}{\rightleftharpoons} MA_3 + A_2 \overset{(R_1)}{\rightleftharpoons} M + 2A_2$$

for which [12]

$$R_H = \frac{2R_2\ (2R_2 + 4R_1)}{2(R_2 + R_1)} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

[12] Wilkins and Williams, *J. Inorg. Nuclear Chem.*, 1958, **6**, 52.
[13] Taube, *Chem. Rev.*, 1952, **50**, 78.
[14] Anderson, Briscoe, and Spoor, *J.*, 1943, 361.
[15] Anderson, Briscoe, Cobb, and Spoor, *J.*, 1943, 367.
[16] Block and Gold, *J.*, 1959, 966.

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Combining (1) and (2) we have

$$R_H = 2R_2 + 2R_{Ni} = 2k_2[\text{Ni en}^{2+}] + 2R_{Ni}$$

We have measured R_H and R_{Ni} at different acidities [Tables 1(*a*) and (*d*)]. The contribution of R_{Ni} towards R_H varies with pH but is always small. This and the constancy of R_H indicates that hydrogen exchange takes place mainly through one-ended bond rupture and that the rate of the latter process is acid-independent in this pH range. Since N–H bond breaking and making (for exchange) is not involved in the rate-determining step (k_2), no hydrogen-isotope effect on the rate would be expected. Further, in most exchanges there is a low concentration of labelled reactant, with which conditions the isotope effect does not enter into the rate equation.[17] For the exchange experiments we must use relatively high reactant concentrations and then $k_2 = 0{\cdot}80 \pm 0{\cdot}12$ min.$^{-1}$ (0·6°).

Weakly Acid Region.—An independent method of obtaining k_2 is from the data on the dependence of k on pH. It can be easily shown from eqn. (2) that, at high enough acidities, a limiting rate for k will be obtained and that this value can be equated to k_2. We

FIG. 3.

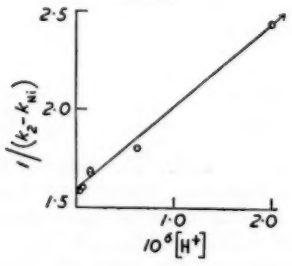
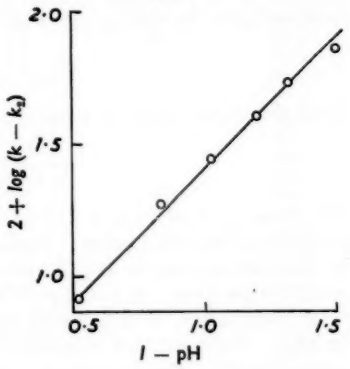


FIG. 4.



observed such a limiting rate [Table 1(*b*) and (*c*) and Fig. 2] and with the reactant concentrations used in the exchange runs we observed $k_2 = 0{\cdot}69 \pm 0{\cdot}03$ min.$^{-1}$ at 0·2°. This is in good agreement with the value from exchange data, the difficulties in obtaining really accurate results for the rapid exchanges being considered. As a corollary to this there should be very slow or no exchange between water and the complex in this limiting region since rupture of one bond and amine exchanges *always* lead to complete and irreversible dissociation. Thus the specific activity of the tritiated amine remains constant at pH 1·5 for nearly one minute (Run 19) which is the longest time the experiment can be carried out because of concomitant loss of complex by dissociation. In this time at pH 6·8 the specific activity of the complex would have fallen by nearly one-half.

We investigated rates in this region also at much lower concentrations of reactants than that above and at constant ionic strength. We used a perchlorate medium since we had observed that chloride and even nitrate enhanced rates. The results are shown in Table 2(*a*). We used these conditions to determine the Arrhenius parameters and found that, for k_2, $E = 20{\cdot}5 \pm 0{\cdot}4$ kcal. mole^{-1} and log $PZ = 16{\cdot}0$ min.$^{-1}$. We also used these reactant concentrations for the determination of k_2 for a variety of amine complexes[18].

We used the hydrogen-ion consumption rate at constant pH as a measure of the dissociation rate in this region. The observation of a first-order rate for over 90% of the reaction, in addition to a final acid consumption corresponding to *both* amino-groups in the

[17] Harris, *Trans. Faraday Soc.*, 1951, **47**, 716.
[18] Shamsuddin Ahmed and Wilkins, unpublished work.

chelate, shows that the intermediate is unstable, and rapidly dissociates further once formed. There is close agreement between the k_2 values obtained by this method and from spectral work at relatively low acidity (Run 30).

Strongly Acid Region.—At pH value below 2, H^+-consumption experiments are no longer sensitive to the liberation of small quantities of amine from the complex. We therefore examined the dissociation spectrally [Table 2(*b*)]. From Fig. 4, which is a linear plot of unit slope, $R = k[\text{Ni en}^{2+}] = \{k_2 + k_2^{H}[H^+]\}[\text{Ni en}^{2+}]$ with $k_2 = 0{\cdot}375$ and $k_2^{H} = 0{\cdot}26$ min.$^{-1}$ at 0·6°.

The acid catalysis could be explained by a pre-equilibrium involving H^+, followed by decomposition of the proton adduct. It is difficult to formulate such a pre-equilibrium involving the amine portion of the molecule, and it is not easy to see why, if the co-ordinated water were involved, this should affect the rate of rupture of bonds. The slightly slower rate in 85% D_2O than in H_2O (runs 35 and 36) does not provide in this case much guidance on the presence of such an equilibrium.[18,19] We favour the idea that the hydrated proton is able, in relatively high concentration, to aid bond rupture directly by competing for the nickel–nitrogen bonding electrons. In low ionic strengths it would be expected that, for charged reactants, log k_2^{H} would vary linearly with the square-root of the ionic strength. At higher ionic strengths the effect usually tails off and, since acid-catalysis is unimportant below about 0·5M-perchloric acid, little effect of ionic strength on the rate is observed.

Summary and General Points.—Our results agree with the idea of stepwise rupture of the ligand from $[\text{Ni en}]^{2+}$ during its dissociation to Ni^{2+}. Since the pK of the intermediate, Ni enH^{3+}, is likely to be less than that [1] of enH_2^{2+} and so have a value of *ca.* 7, then at pH 7 the free nitrogen of the intermediate will exist to an important extent as the free amino-group and the tendency to re-form chelate is then greater than that of further breakage. Thus the *overall* rate of dissociation is much less than at pH 5 where, because the intermediate must be present mainly as the acid form, re-formation is much slower, dissociation depending only on the relatively fast, rate-determining, first bond rupture. The idea of a complex containing unidentate ethylenediamine is not new and has been invoked, for example, as a chemical intermediate in recent kinetic studies.[20,21] Schläfer and Kling [21] have studied spectrophotometrically the dissociation of $[\text{Cr en}_3]^{3+}$ to $[\text{Cr en}_2(H_2O)_2]^{3+}$ and postulated the existence of a stable intermediate during the reaction which, they suggest, might be a "one-end attached" species. However, Bjerrum, Jörgensen, and Nielsen [22] maintain that Schläfer and Kling's results can be as easily explained on the basis of a *labile* intermediate of constitution $[\text{Cr en}_2(\text{enH})(H_2O)]^{4+}$. The subsequent dissociation of $[\text{Cr en}_2(H_2O)_2]^{3+}$ has been studied, and stable chemical intermediates have been suggested here also.[23]

The fact that the bond-rupture rate constant k_2 is measurable indicates that the enhanced kinetic stability of chelates compared with unidentate-containing complexes (*e.g.*, in this case ammonia complexes) does not result solely from this ability to sever and re-form a single bond before complete cleavage. In fact, in our work only a factor of about twenty (ratio of the two limiting rate constants) is thus introduced. It must therefore be easier to remove an ammonia molecule from the environment of the nickel ion than an $-NH_2$ ligand when it is attached *via* another group also. In the latter case, to constitute severance in a kinetic sense it may be that the aliphatic chain must twist so that the $-NH_2$ group is rotated away from the metal atom. The k_1 step is more analogous to $Ni-NH_3$ cleavage and we know this is fast. As well as a water molecule (as we believe) opening up the first bond (k_2), in higher acidities the hydrated proton can also aid bond

[19] Bell, "Acid–Base Catalysis," Oxford, 1941; Wiberg, *Chem. Rev.*, 1955, **55**, 713.
[20] Gehman and Fernelius, *J. Inorg. Nuclear Chem.*, 1959, **9**, 71.
[21] Schläfer and Kling, *Z. phys. Chem.* (*Leipzig*), 1958, **16**, 14.
[22] Bjerrum, Jörgensen, and Nielsen, reported at International Conference on Co-ordination Compounds, London, 1959, Paper 101.

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rupture (k_2^H) although its contribution to the effect below 3M is never overwhelming. It is apparent then that acid can enhance the overall dissociation rate of $[Ni\ en]^{2+}$ in two ways: at lower acidity, by altering the form of the intermediate, and at high acidities, more directly, by increasing the value of k_2.

Our results are compared in Table 3 with those of Bjerrum, Poulsen, and Poulsen in methanol.[4] The latter are results extrapolated to 0° from measurements at much lower temperatures. Considering the experimental difficulties and the preliminary nature of the methanol work, apart from the change in medium, we feel that the agreement is quite good. Certainly the observed sequence of a gradually slowing dissociation as ligands are removed from the tris-species to the free metal ion has been confirmed in our work. The only other chelate amine systems which have been similarly studied, phenanthroline-nickel [6] and ethylenediaminechromium [21,23] show a similar characteristic.

TABLE 3. *Kinetic data for successive dissociation of* $[Ni\ en_3]^{2+}$.

Change	Rate constant (0·0°) in 0·1–0·5M-acid (sec.$^{-1}$)	
	This work	Methanol
$[Ni\ en_3]^{2+} \longrightarrow [Ni\ en_2]^{2+}$	>0·1 (ref. 3)	8·0
$[Ni\ en_2]^{2+} \longrightarrow [Ni\ en]^{2+}$	~0·1	0·6
$[Ni\ en]^{2+} \longrightarrow Ni^{2+}$	0·01	0·1

The pattern of behaviour with pH observed here has been confirmed for several similar compounds.[18] We hope to extend our approach to mono-complexes containing an unsymmetrical bidentate ligand (*e.g.*, both a primary and a tertiary amine) so that we might in this way determine the relative tendencies of the two ends to dissociation.

We thank Drs. W. C. E. Higginson and M. J. G. Williams for discussions, and the Pakistan Government for a maintenance grant.

THE UNIVERSITY, SHEFFIELD. [*Received, April 22nd,* 1959.]

[23] Schläfer and Kollrack, *Z. phys. Chem.*, 1958, **18**, 348.

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752. *The Ehrlich–Sachs Reaction. Part II.*[1]

By D. M. W. ANDERSON and F. BELL.

Although normally one molecule of the nitroso-compound reacts with one molecule of the methylene compound it is now shown that other modes of reaction are possible.

The products of reaction of nitrosobenzene with malononitrile and with nitromethane are identified.

The infrared spectra of these compounds are outlined.

IN Part I it was shown that the primary product (I) of the interaction of an aromatic nitroso-compound, such as *NN*-dimethyl-*p*-nitrosoaniline, with cyanoacetamide was liable to react with the alcohol used as solvent to give, by elimination of hydrocyanic acid, an alkoxyacetamide (II). It is now found that the α-substituted cyanoacetic ester (III), produced initially from interaction of an aromatic nitroso-compound with a cyanoacetic ester, is liable to interact with another molecule of the ester to give a cyano-diester (IV) or, as indicated by the infrared spectra, more probably (V). This reaction goes so readily with *NN*-diethyl-*p*-nitrosoaniline that it has not been possible to isolate an intermediate of type (III). In other examples the intermediate (III) is the preferred product but a slow further condensation can be brought about in warm alcohol in the presence of potassium carbonate.

[1] Part I, *J.*, 1957, 516.

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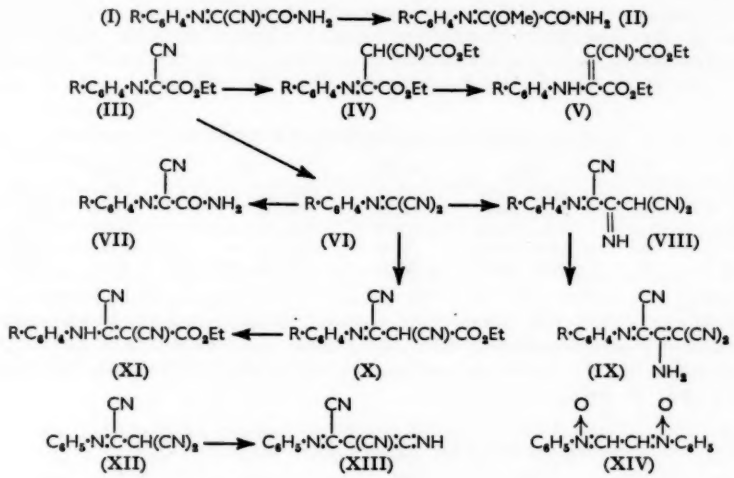
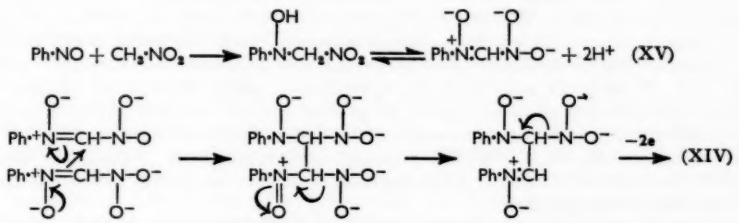
From the interaction of *NN*-dimethyl-*p*-nitrosoaniline and ethyl cyanoacetate compounds (III; R = NMe_2) and (IV or V; R = NMe_2) have been isolated and, rather unexpectedly, *N*-dicyanomethylene- (VI; R = NMe_2) and *N*-carbamoylcyanomethylene-*N'N'*-dimethyl-*p*-phenylenediamine (VII; R = NMe_2). Similarly the dicyano-compound (VI; R = NEt_2) was isolated from interaction of *NN*-diethyl-*p*-nitrosoaniline and ethyl cyanoacetate.

When compounds (VI) are prepared from the appropriate nitroso-compound and malononitrile they are accompanied by traces of dark-blue compounds (IX), probably



produced *via* (VIII). They are readily prepared by the interaction of the dicyano-compounds (VI) and malononitrile or of the nitroso-compound and malononitrile dimer (2-amino-1,1,3-tricyanopropene) [2] in the presence of potassium carbonate. On the other hand, the dicyanomethylene compounds (VI) react with cyanoacetates to yield dicyano-esters (X) or (XI). These are analogous to (XII) or (XIII), a strongly acidic compound obtained by the interaction of nitrosobenzene with malononitrile.

Nitrosobenzene with nitromethane gives a bright yellow compound (XIV). The authors are indebted to one of the referees for the suggestion that it is formed from the primary product of condensation (XV) by a dimerisation somewhat akin to those described by Bamberger [3] and by Hellmann and Teichmann.[4]



[2] Carboni, Coffman, and Howard, *J. Amer. Chem. Soc.*, 1958, **80**, 2838.
[3] Bamberger, *Ber.*, 1900, **33**, 941.
[4] Hellmann and Teichmann, *Chem. Ber.*, 1956, **89**, 1134.

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The structure was confirmed by synthesis from glyoxal and phenylhydroxylamine; it is comparable with *N*-cinnamylideneaniline *N*-oxide, which was prepared by the interaction of cinnamaldehyde with phenylhydroxylamine.[5]

Experimental

The infrared spectra were determined in Nujol and hexachlorobutadiene mulls on a Hilger H 800 spectrophotometer fitted with sodium chloride and lithium fluoride prisms. Results are recorded in $cm.^{-1}$.

Ehrlich–Sachs Amides.—N-*Carbamoylcyanomethylene*-N′N′-*di*-n-*propyl*-p-*phenylenediamine*, produced by the interaction of *p*-nitroso-*NN*-di-n-propylaniline with cyanoacetamide in presence of potassium carbonate, crystallised from ethanol in fine, red needles, m. p. 148—151° (Found: C, 65·8; H, 6·9. $C_{15}H_{20}ON_4$ requires C, 66·2; H, 7·3%).

Infrared spectra of 4,2,1-$R_2N{\cdot}C_6H_3R'{\cdot}N{:}C(CN){\cdot}CO{\cdot}NH_2$.

R	R′	NH_2	−C⋮N	CO	>C:N−	
Et	H	3430, 3180	2210	1687 (s)	1618	1505
Me	H	3440, 3200	2220	1690 (s)	1625	1550, 1520
Me	Me	3440, 3160	2200	1682 (s)	1615	1593, 1520
Et	Me	3440, 3150	2200	1681 (s)	1615	1593, 1500
Pr^n	H	3360, 3190	2200	1714 (w), 1657 (s)	1615	1542, 1525

Ehrlich–Sachs Esters.—(a) *From tertiary bases.* N-(α-*Cyano*-α-*ethoxycarbonylmethylene*)-N′,N′,2-*trimethyl*-p-*phenylenediamine*, from *N*,*N*,3-trimethyl-4-nitrosoaniline and ethyl cyanoacetate in ethanol (K_2CO_3), formed red needles, m. p. 118° (Found: C, 64·7; H, 6·2. $C_{14}H_{17}O_2N_3$ requires C, 64·8; H, 6·6%).

Infrared spectra of 4,2,1-$R_2N{\cdot}C_6H_3R'{\cdot}N{:}C(CN){\cdot}CO_2R''$.

R	R′	R″	−C⋮N	CO	>C:N−	
Pr^n	H	Me	2195	1737(s)	1615	1530
Me	H	Et	2200	1740(s)	1618	1530
Me	Me	Et	2205	1705(s)	1622	1520
Me	Me	Me	2200	1705(s)	1617	1520
Me	H	Me	2220	1708(s)	1625	1540, 1515
Et	Me	Me	2200	1755(w), 1693(s)	1615	1515
Et	Me	Et	2200	1694(s)	1615	1515

(b) *From secondary bases.* N-(α-*Cyano*-α-*methoxycarbonylmethylene*)-N′-*ethyl*-p-*phenylenediamine*, from *N*-ethyl-*p*-nitrosoaniline and methyl cyanoacetate in methanol (K_2CO_3), formed red needles, m. p. 157°, from ethanol (Found: C, 62·3; H, 5·2. $C_{12}H_{13}O_2N_3$ requires C, 62·4; H, 5·6%). N-(α-*Cyano*-α-*ethoxycarbonylmethylene*)-N′-*ethyl*-p-*phenylenediamine*, from *N*-ethyl-*p*-nitrosoaniline and ethyl cyanoacetate in ethanol (K_2CO_3), formed orange needles, m. p. 106—107°, after elution from alumina by ethyl acetate and subsequent recrystallisation from benzene (Found: C, 63·9; H, 5·5. $C_{13}H_{15}O_2N_3$ requires C, 63·7; H, 6·1%). N-(α-*Cyano*-α-*methoxycarbonylmethylene*)-N′-*methyl*-p-*phenylenediamine*, from *N*-methyl-*p*-nitrosoaniline and methyl cyanoacetate in methanol (K_2CO_3), crystallised from benzene in orange needles, m. p. 170° (Found: C, 61·6; H, 5·1. $C_{11}H_{11}O_2N_3$ requires C, 60·8; H, 5·1%). The mother-liquor deposited dark blue prisms of an *isomer*, m. p. 168° (Found: C, 60·9; H, 4·9%), which was slowly transformed into the orange compound by boiling chloroform or benzene. *N*-(α-Cyano-α-ethoxycarbonylmethylene)-*N*′-methyl-*p*-phenylenediamine, from *N*-methyl-*p*-nitrosoaniline and ethyl cyanoacetate (K_2CO_3), crystallised from ethanol in purple prisms, m. p. 136°, in agreement with Sachs and Bry.[6]

Ehrlich–Sachs Dinitriles.—*N*-Dicyanomethylene-*N*′*N*′-diethyl-, m. p. 114°, and *N*-dicyanomethylene-*N*′*N*′-dimethyl-*p*-phenyldiamine, m. p. 167°, were prepared by Sachs's method.[7]

[5] Bamberger and Weitnauer, *Ber.*, 1922, **55**, 3381.
[6] Sachs and Bry, *Ber.*, 1901, **34**, 120.
[7] Sachs, *Ber.*, 1900, **33**, 964.

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Infrared spectra of $RNH\cdot C_6H_4\cdot N{:}C(CN)\cdot CO_2R'$.

R	R'	NH	$-C{\equiv}N$	CO	$>C{:}N-$	
Et	Et	3400	2220	1750(s)	1625	1535
Et	Me	3350	2210	1731(s)	1628	1544
Me	Et	3330	2215	1741(s)	1627	1548
Me	Me (yellow)	3410	2210	1713(s)	1630	1552, 1508
Me	Me (blue)	3410	2215	1733(m), 1706(m)	1622	1580, 1544

N-*Dicyanomethylene*-N'-*ethyl*-N'-*methyl*-p-*phenylenediamine* was obtained by boiling an ethanolic solution of *N*-ethyl-*N*-methyl-*p*-nitrosoaniline (2·4 g.) and malononitrile (1·2 g.) for ¾ hr. On cooling, the solution deposited dark-violet crystals, which contained a small amount of an intensely blue compound, sparingly soluble in ethyl acetate. This impurity was removed completely on alumina, yielding red needles, m. p. 128° (Found: C, 67·9; H, 5·6. $C_{12}H_{12}N_4$ requires C, 67·9; H, 5·7%).

N-*Dicyanomethylene*-N'N'-*diethyl*-2-*methyl*-p-*phenylenediamine*. An ethanolic solution of *NN*-diethyl-3-methyl-4-nitrosoaniline and malononitrile was boiled for ¾ hr. and filtered from a small deposit of dark-blue needles, m. p. *ca.* 200° (decomp.). The filtrate deposited material, an ethyl acetate solution of which was passed through alumina. The *dicyanide* recovered from the first fraction formed prisms, m. p. 130°, from ethanol (Found: C, 70·0; H, 6·5. $C_{14}H_{16}N_4$ requires C, 70·0; H, 6·7%).

N-*Dicyanomethylene*-N',N',2-*trimethyl*-p-*phenylenediamine*. *N*,*N*,3-Trimethyl-4-nitrosoaniline was heated with malononitrile in ethanol; after ¾ hr. the crystals were filtered off and recrystallised from ethyl acetate, yielding purple needles, m. p. 208° (Found: C, 68·2; H, 5·5. $C_{12}H_{12}N_4$ requires C, 67·9; H, 5·7%). More of this *dicyanide*, in a slightly less pure condition, was obtained from the ethanolic filtrate.

Infrared spectra of $4,2,1\text{-}RR'N\cdot C_6H_3R''\cdot N{:}C(CN)_2$.

R	R'	R''	$-C{\equiv}N$	$>C{:}N-$	
Me	Me	H	2226, 2212	1625	1540
Me	Et	H	2206, shoulder 2203	1615	1530
Et	Et	Me	2212, 2208	1616	1522
Me	Me	Me	2205, 2202	1620	1520
Et	Et	H	2204 (1 peak only)	1615	1530

Condensations involving 2 Mols. of Ester.—N-(2-*Cyano*-1,2-*dimethoxycarbonylvinyl*)-N'N'-*diethyl*-p-*phenylenediamine*. Freshly heated potassium carbonate (3 g.) was added to a mixture of *NN*-diethyl-*p*-nitrosoaniline (2·5 g.) and methyl cyanoacetate (2 c.c.) in methanol (15 c.c.). After 1 hr. water was stirred in and the black oil separated by decantation. The oil was dissolved in warm ethanol and the crystals which separated on cooling were purified by repeated crystallisation from ethanol or ethyl acetate, yielding the *cyano-ester* as yellow prisms, m. p. 152° (Found: C, 61·7; H, 6·3; N, 12·6; O, 19·3. $C_{17}H_{21}O_4N_3$ requires C, 61·7; H, 6·3; N, 12·7; O, 19·3%). It was readily soluble in warm, dilute sodium hydroxide from which it was reprecipitated by acetic acid; it could be recovered after solution in boiling acetic anhydride or cold concentrated hydrochloric acid.

By the same method the following *p*-phenylenediamines were obtained in small yield: N-(2-*Cyano*-1,2-*diethoxycarbonylvinyl*)-N'N'-*diethyl*-, as yellow prisms, m. p. 126° (Found: C, 64·0; H, 7·2; N, 11·7; O, 17·4. $C_{19}H_{25}O_4N_3$ requires C, 63·5; H, 7·0; N, 11·7; O, 17·8%), from *NN*-diethyl-*p*-nitrosoaniline and ethyl cyanoacetate. N-(2-*Cyano*-1,2-*dimethoxycarbonylvinyl*)-N'N'-*dimethyl*-, as yellow prisms, m. p. 122°(Found: C, 59·5; H, 5·6; N, 13·8. $C_{15}H_{17}O_4N_3$ requires C, 59·4; H, 5·6; N, 13·8%), from *NN*-dimethyl-*p*-nitrosoaniline and methyl cyanoacetate. Chromatography of the crude product in ethyl acetate on alumina led to the isolation of *N*-dicyanomethylene-*N'N'*-dimethyl-*p*-phenylenediamine and *N*-carbamoylcyanomethylene-*N'N'*-dimethyl-*p*-phenylenediamine in addition to the previously described [1] *pp'*-dimethylaminoazoxybenzene and *N*-(α-cyano-α-ethoxycarbonylmethylene)-*N'N'*-dimethyl-*p*-phenylenediamine. This dicyanide was obtained when a mixture of *N*-(α-cyano-α-methoxycarbonylmethylene)-*N'N'*-dimethyl-*p*-phenylenediamine (1·5 g.), methyl cyanoacetate (1·5 c.c.),

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potassium carbonate (3 g.), and methanol (15 c.c.) was gently warmed for ½ hr. and poured into water. The sticky black product was repeatedly recrystallised from ethanol. N-(2-*Cyano*-1,2-*diethoxycarbonylvinyl*)-N'N'-*dimethyl*-, as yellow needles, m. p. 118° (Found: C, 62·0; H, 6·1. $C_{17}H_{21}O_4N_3$ requires C, 61·6; H, 6·3%), from *NN*-dimethyl-*p*-nitrosoaniline and ethyl cyanoacetate. N-(2-*Cyano*-1,2-*dimethoxycarbonylvinyl*)-N'-*ethyl*-N'-*methyl*-, as yellow prisms, m. p. 103—105° (Found: C, 61·1; H, 5·9. $C_{16}H_{19}O_4N_3$ requires C, 60·6; H, 6·0%), from *N*-ethyl-*N*-methyl-*p*-nitrosoaniline and methyl cyanoacetate. N-(2-*Cyano*-1,2-*diethoxycarbonylvinyl*)-N'-*ethyl*-N'-*methyl*-, as yellow plates, m. p. 116—118° (Found: C, 62·7; H, 7·0. $C_{18}H_{23}O_4N_3$ requires C, 62·6; H, 6·7%), from *N*-ethyl-*N*-methyl-*p*-nitrosoaniline and ethyl cyanoacetate. N-(2-*Cyano*-1,2-*diethoxycarbonylvinyl*)-N',N',2-*trimethyl*-, as needles, m. p. 138° (Found: C, 62·7; H, 6·7. $C_{18}H_{23}O_4N_3$ requires C, 62·6; H, 6·7%), by the interaction of ethyl cyanoacetate with *N*-(α-cyano-α-ethoxycarbonylmethylene)-*N'*,*N'*,2-trimethyl-*p*-phenylenediamine in ethanol (K_2CO_3). It was purified by elution from alumina by ethyl acetate, solution in dilute sodium hydroxide, reprecipitation by acetic acid, and subsequent crystallisation from ethanol.

Infrared spectra of 4,2,1-RR'N·C_6H_3R''·NH·C(CO_2R''')·C(CN)·CO_2R'''.

R	R'	R''	R'''	NH	−C≡N	CO	C=C	
Me	Me	H	Me	3290	2220	1765(s), 1680(s), 1720(w)	1620	1600, 1575, 1530
Me	Me	H	Et	3260	2220	1760(s), 1672(s)	1617	1587, 1568, 1527
Me	Et	H	Et	3255	2220	1755(s), 1670(s)	1612	1580, 1560, 1510
Me	Et	H	Me	3265	2220	1755(s), 1675(s)	1615	1590, 1567, 1520
Et	Et	H	Me	3280	2230	1760(s), 1680(s)	1620	1600, 1575, 1530
Et	Et	H	Et	3250	2235	1762(s), 1680(s)	1620	1590, 1570, 1530
Me	Me	Me	Et	3270	2230	1760(s), 1675(s)	1622	1590, 1525

Condensations between Dinitriles and Esters.—A mixture of *N*-dicyanomethylene-*N'*-ethyl-*N'*-methyl-*p*-phenylenediamine (0·5 g.), methyl cyanoacetate (0·5 c.c.), potassium carbonate, and methanol (15 c.c.) was warmed for ½ hr., then diluted with water, and left overnight. The aqueous layer was decanted and the residue purified by repeated recrystallisation from ethanol, giving N-(1,2-*dicyano*-2-*methoxycarbonylvinyl*)-N'-*ethyl*-N'-*methyl*-p-*phenylenediamine* in golden-red needles, m. p. 120—122° (Found: C, 63·2; H, 5·5. $C_{15}H_{16}O_2N_4$ requires C, 63·4; H, 5·6%). The *ethyl ester* was similarly obtained from ethyl cyanoacetate and formed orange-red plates, m. p. 130—133° (Found: C, 64·4; H, 5·8. $C_{16}H_{18}O_2N_4$ requires C, 64·4; H, 6·2%). These compounds yielded almost colourless sparingly soluble hydrochlorides, from which they could be regenerated.

In the same way the following *p*-phenylenediamines were obtained: N-(1,2-*dicyano*-2-*ethoxycarbonylvinyl*)-N'N'-*diethyl*-, dark red-brown prisms, m. p. 133—136°, from ethanol (Found: C, 65·5; H, 6·2. $C_{17}H_{20}O_2N_4$ requires C, 65·4; H, 6·4%); N-(1,2-*dicyano*-2-*methoxycarbonylvinyl*)-N'N'-*dimethyl*-, red prisms, m. p. 158—160°, from ethyl acetate (Found: C, 62·7; H, 5·4; $C_{14}H_{14}O_2N_4$ requires C, 62·2; H, 5·2%); N-(1,2-*dicyano*-2-*ethoxycarbonylvinyl*)-N'N'-*dimethyl*-, orange-red prisms, m. p. 170—174°, from ethyl acetate (Found: C, 63·3; H, 5·6. $C_{15}H_{16}O_2N_4$ requires C, 63·4; H, 5·6%); N-(1,2-*dicyano*-2-*methoxycarbonylvinyl*)-N'N'-*diethyl*-, canary-yellow plates, m. p. 122—124°, from ethanol (Found: C, 64·6; H, 6·4; N, 18·7. $C_{16}H_{18}O_2N_4$ requires C, 64·4; H, 6·0; N, 18·8%). This compound is a striking example of dimorphism. If the

Infrared spectra of RR'N·C_6H_4·NH·C(CN)·C(CN)·CO_2R''.

R	R'	R''	NH	−C≡N	CO	C=C	
Et	Et	Et	3240	2220	1682	1612	1588, 1522
Me	Me	Et	3220	2215	1685	1610	1582, 1525
Me	Me	Me	3200, 3165	2210	1688	1610	1562, 1522
Me	Et	Me	3270	2235	1692	1612	1590, 1520

yellow plates are subjected to pressure they become red; if the yellow form is recrystallised from carbon tetrachloride the compound separates in red prisms.

Condensation Products corresponding to Malononitrile Dimer.—(*a*) Anhydrous potassium carbonate (5 g.) was added to a mixture of malononitrile (1 g.) and *NN*-diethyl-*p*-nitrosoaniline (2·7 g.) in methanol (15 c.c.). After the brisk reaction water was added; the sticky precipitate

was heated with ethanol to remove impurities. The residue was extracted (Soxhlet) with ethyl acetate to yield N-(2-*amino*-1,3,3-*tricyanoallylidene*)-N′N′-*diethyl*-p-*phenylenediamine* as dark-blue crystals, m. p. 232° (decomp.) (Found: C, 65·9; H, 5·6; N, 28·3. $C_{16}H_{16}N_6$ requires C, 65·7; H, 5·5; N, 28·8%). (*b*) *N*-Ethyl-*p*-nitrosoaniline was used as in (*a*); the resultant N-(2-*amino*-1,3,3-*tricyanoallylidene*)-N′-*ethyl*-p-*phenylenediamine* crystallised from aqueous pyridine or " Cellosolve " in dark-violet plates, m. p. 230° (decomp.) (Found: C, 63·4; H, 4·6; N, 31·5. $C_{14}H_{12}N_6$ requires C, 63·7; H, 4·5; N, 31·8%). (*c*) *NN*-Dimethyl-*p*-nitrosoaniline was used as in (*a*); the resultant N-(2-*amino*-1,3,3-*tricyanoallylidene*)-N′N′-*dimethyl*-p-*phenylenediamine* crystallised from a large bulk of acetone as a dark-violet powder, m. p. 256° (decomp.) (Found: C, 63·7; H, 4·3; N, 31·7. $C_{14}H_{12}N_6$ requires C, 63·7; H, 4·5; N, 31·8%).

The same products were obtained when malononitrile dimer (2-amino-1,1,3-tricyanopropene) was used in place of malononitrile.

Infrared spectra of $RR'N{\cdot}C_6H_4{\cdot}N{:}C(CN){\cdot}C(NH_2){:}C(CN)_2$.

R	R′	NH_2	$-C{\equiv}N$	$>C{:}N$
Et	Et	3390, 3280, 3190	2212, 2204	1608
Me	Et	3390, 3200, 3195	2226, 2212	1610
Me	Me	3380, 3265, 3180	2206, 2190	1615 shoulder, 1600
H	Et	3380, 3290, 3200	2218, 2200	1615

Condensation of Nitrosobenzene with Malononitrile.—Potassium carbonate (4 g.) was added to a mixture of nitrosobenzene (2 g.), malononitrile (1·4 g.), and methanol (15 c.c.). After the brisk reaction the mixture was decomposed by water and submitted to one of the following treatments: (*a*) The mixture was left in the refrigerator overnight, and the deposited potassium salt then filtered off, dried on paper, and then boiled with chloroform. The residual salt was dissolved in water and decomposed by hydrochloric acid, and the precipitate recrystallised from acetic acid or chloroform. (*b*) The mixture was shaken with ether and then the aqueous solution was acidified with hydrochloric acid. 1,1,2-*Tricyano*-2-*phenyliminoethane* (XII) was obtained in large, pale-yellow prisms, which decomposed indefinitely at *ca.* 170° (Found: C, 68·5; H, 3·0; N, 28·8. $C_{11}H_6N_4$ requires C, 68·0; H, 3·1; N, 28·9%). The compound has a dissociation constant approximately three times that of acetic acid, and shows the following bands in the infrared spectrum: 3290(w), 3220(m), 3120(s), 2218(s), 2212(s), 2207(s), 1613(vs), 1582(vs). The potassium salt has bands at 2212(s), 2198(s), 1550(sh), 1538(vs).

The Interaction of Nitrosobenzene with Nitromethane.—Potassium carbonate (3 g.) was added to a mixture of nitromethane (1 g.) and nitrosobenzene (2 g.) in methanol. The dark oil that separated on addition of water was washed with ethanol to yield a small amount of solid, which after repeated recrystallisation from ethyl acetate gave *glyoxal di*(*phenyliso-oxime*) (XIV) as yellow needles, m. p. 184—186° (Found: C, 70·1, 70·3; H, 5·1, 4·9; N, 11·8, 11·6; O, 13·2. $C_{14}H_{12}O_2N_2$ requires C, 70·0; H, 5·0; N, 11·7; O, 13·3%). It could be recovered from boiling acetic anhydride, was insoluble in hot dilute sodium hydroxide or hot dilute hydrochloric acid, and gave an orange-yellow solution in concentrated sulphuric acid. It was also prepared as follows. An aqueous solution of glyoxal bisulphite was added to an ethanolic solution of phenylhydroxylamine and the mixture warmed on a steam bath for a few minutes. On cooling there was deposited a brown mass which was separated by decantation and dissolved in hot ethanol. The crop was recrystallised from ethyl acetate, giving material of the same m. p. and infrared spectrum as (XIV). The principal bands in the infrared spectrum were: 1505(m), 1330(s), 1295(m), 1185(m), 1170(m), 1157(m), 1087(m), 1072(m), 815(m), 775(s). This may be compared with the spectrum of cinnamylideneaniline oxide, with bands at 1515(m), 1335(m), 1300(m), 1180(m), 1170(sh), 1155(m), 1050(s), 968(s), 910(m), 755(s), 730(s).

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XUM

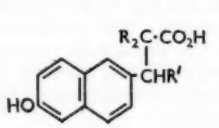
753. *Œstrogenic Carboxylic Acids. Part II.* Open-chain Analogues of Doisynolic Acid.*

By Edward R. Clark and R. D. Robson.

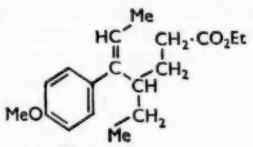
A number of alkyl-substituted 5-*p*-methoxyphenyl-pentanoic and -pentenoic acids have been synthesised. None was superior in œstrogenic activity to the previously reported ethyl 3-ethyl-4-*p*-methoxyphenylhex-4-ene-1-carboxylate.

Jacques and Horeau [1] have shown that, whereas allenolic acid [β-(6-hydroxy-2-naphthyl)-propionic acid] (I; R = R′ = H) is inactive, β-ethyl-αα-dimethylallenolic acid (I; R = Me, R′ = Et) is a potent œstrogen. Similarly in the bisdehydrodoisynolic acid series, absence of alkyl groups at positions 1 and 2 markedly decreases the potency.[2] It was hoped, therefore, that introduction of alkyl groups at positions 1 and 2 of ethyl 3-ethyl-4-*p*-methoxyphenylhex-4-ene-1-carboxylate [3] (II) would enhance the œstrogenic activity.

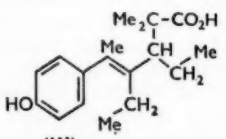
One of the two possible optical isomers of the acid (III) bears a particularly close formal resemblance to bisdehydrodoisynolic acid. Its synthesis could, we believed, be achieved by a Reformatsky reaction between ethyl α-bromoisobutyrate and 4-ethyl-5-*p*-methoxyphenylhexan-3-one (V; R = R′ = Et, R″ = Me), the double bond of the derived hexene (VII) being expected to migrate into conjugation with the ring.



(I)



(II)



(III)

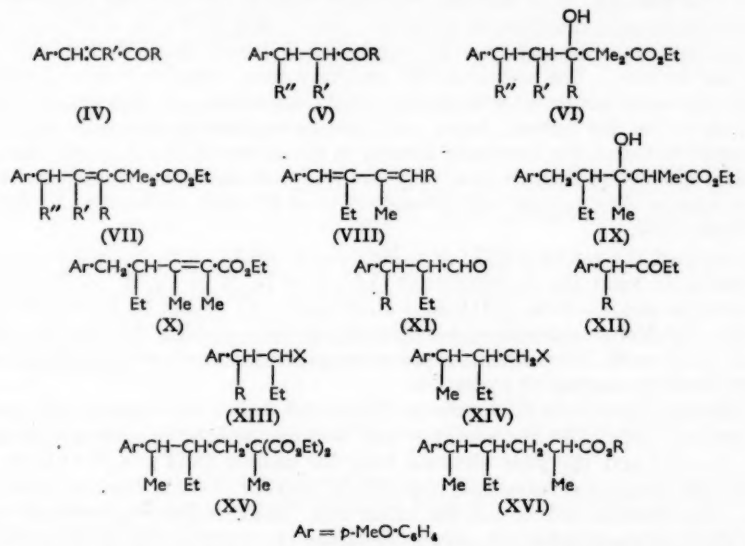
For a preliminary investigation the most readily available ketone of type (V) appeared to be 3-ethyl-4-*p*-methoxyphenylhexan-2-one (V; R = Me, R′ = R″ = Et) which has been prepared by the action of ethylmagnesium bromide on α-ethyl-4-methoxystyryl methyl ketone [4] (IV; R = Me, R′ = Et). Use of methylmagnesium bromide and iodide in this reaction, in attempts to obtain the analogue (V; R = R″ = Me, R′ = Et) was not successful; the butadiene (VIII; R = H), $\lambda_{max.}$ 275 mμ (ε 13,700) in alcohol, formed by 1,2-addition, was the only isolable product when the bromide was used; only a very small amount of the required 1,4-addition product was obtained by using methylmagnesium iodide in the presence of cuprous chloride, which is stated to promote 1,4-addition.[5] Shukis and Ritter [4] state that some 1,2-addition also occurs with ethylmagnesium bromide. Our product was shown by infrared analysis to be a saturated ketone ($\nu_{max.}$ 1709 cm.$^{-1}$), there being no absorption due to hydroxyl or αβ-unsaturated ketone groups, but presence of the diene (VIII; R = Me) in the product was demonstrated by the ultraviolet absorption of an alcohol solution, a peak occurring at 277 mμ ($E^{1\%}_{1\,cm.}$ 403); the absence of a peak or inflexion at 296·5 mμ confirmed the absence of the original unsaturated ketone. Fractional distillation failed to separate the saturated ketone from the diene, which, however, would not be expected to interfere with a Reformatsky reaction. None of the required products were obtained, however, on treating this mixture with ethyl α-bromoisobutyrate, α-bromopropionate, or α-bromoacetate. Examination of molecular models demonstrated that the carbonyl group of 3-ethyl-4-*p*-methoxyphenylhexan-2-one (V;

* *J.*, 1950, 3397 is to be considered as Part I.

[1] Jacques and Horeau, *Bull. Soc. chim. France*, 1948, 711.
[2] Heer and Miescher, *Helv. Chim. Acta*, 1945, **28**, 1506.
[3] Clark, *J.*, 1950, 3397.
[4] Shukis and Ritter, *J. Amer. Chem. Soc.*, 1950, **72**, 1488.
[5] Kharasch and Tawney, *ibid.*, 1941, **63**, 2308.

R = Me, R′ = R″ = Et) is shielded but that the absence of either of the two ethyl groups makes it more accessible.

Catalytic hydrogenation of the styryl ketone (IV; R = Me, R′ = Et) and oxidation of the product with chromic acid gave 3-4′-methoxybenzylpentan-2-one (V; R = Me, R′ = Et, R″ = H) which reacted in the expected manner with ethyl α-bromopropionate, and α-bromoisobutyrate in the presence of zinc. The ethyl 3-hydroxy-4-4′-methoxybenzyl-3-methylhexane-2-carboxylate (IX) formed from the α-bromopropionate was partly dehydrated during isolation to the αβ-unsaturated ester (X), and dehydration was completed with potassium hydrogen sulphate. The position of the double bond was established by the infrared spectrum (strong band at 1730 cm.$^{-1}$). Dehydration of the crude product of reaction between the pentanone (V; R = Me, R′ = Et, R″ = H) and ethyl α-bromoisobutyrate gave ethyl 2,3-dimethyl-4-4′-methoxybenzylhex-3-ene-2-carboxylate (VII; R = Me, R′ = Et, R″ = H), the absence of an absorption peak at *ca.* 250 mμ showing that the double bond was not in conjugation with the aromatic ring, and this was confirmed by the weakness of the infrared absorption at *ca.* 1575 cm.$^{-1}$.



Ar = p-MeO·C$_6$H$_4$

Even in the successful Reformatsky reactions the yields were poor. It was hoped that better yields of related compounds (*e.g.*, VII; R = H, R′ = R″ = Et) would be obtained from the aldehydes (XI).

Various approaches were tried for synthesis of these aldehydes. Darzens glycidic ester condensations of the ketones (XII; R = Me and Et), with either ethyl chloroacetate in the presence of sodium methoxide or ethyl dichloroacetate in the presence of magnesium–mercury amalgam, were unsuccessful, as was an attempt to prepare ethyl αβ-epoxy-α-ethyl-β-*p*-methoxyphenylbutyrate and hence 2-*p*-methoxyphenylpentan-3-one from 4-methoxyacetophenone and ethyl α-bromobutyrate. These ketones (XII; R = Me and Et) were obtained from 1-*p*-methoxyphenylbutan-2-one [6] (XII; R = H).

The ketones (XII; R = Et or Me) were converted *via* the alcohols into the halides (XIII; R = Et, X = Br; and R = Me, X = Cl). The derived Grignard reagents were then treated with ethyl orthoformate, and the products were hydrolysed. None of the expected aldehyde was obtained from the bromohexane (XIII; R = Et, X = Br), and

[6] Myers, Pratt, Morgan, O'Donnell, and Jensen, *J. Amer. Chem. Soc.*, 1955, **77**, 5655.

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only a very small amount of the aldehyde (XI; R = Me) (as its 2,4-dinitrophenylhydrazone) was obtained from the chloropentane (XIII; R = Me, X = Cl). In contrast, 4-methoxyphenethyl chloride yielded β-*p*-methoxyphenylpropionaldehyde in 23% yield by an analogous process. The virtual failure of the secondary Grignard reagent to react with ethyl orthoformate is similar to the failure to obtain an aldehyde from the reaction of isopropyl-lithium with *NN*-dimethylformamide.[7]

Brown and McFarlin [8] have described an elegant method for the reduction of acid chlorides to aldehydes using lithium tri-t-butoxyaluminium hydride. When our work was done the method had not been applied to aliphatic acid chlorides, though a more recent paper [9] describes its successful application to some straight-chain aliphatic acid chlorides. We attempted reduction of α-ethyl-β-*p*-methoxyphenylbutyryl chloride by this reagent. The corresponding ethyl butenoate was obtained from 4-methoxyacetophenone and ethyl α-bromobutyrate, hydrolysed to the free acid, and reduced in alkaline solution with nickel–aluminium alloy. The chloride of the product failed to yield an identifiable product when treated with lithium tri-t-butoxyaluminium hydride.

The aldehyde (XI; R = Me) was eventually prepared by oxidising the corresponding alcohol with chromic anhydride in pyridine. The alcohol (XIV; X = OH) was obtained from the butenoate by catalytic hydrogenation followed by reduction with lithium aluminium hydride. The hydrogenation was very slow, owing to traces of sulphur impurities, even after treatment with Raney nickel. In subsequent runs initial reduction of the butenoate to the butenol before catalytic hydrogenation overcame this difficulty. An attempt to reduce the butenoate directly to the alcohol (XIV; X = OH) by an excess of lithium aluminium hydride gave only 2-ethyl-3-*p*-methoxyphenylbut-2-en-1-ol, which with manganese dioxide gave only a small yield of aldehyde, isolated as its 2,4-dinitrophenylhydrazone.

As expected, the aldehyde (XI; R = Me) reacted readily with zinc and ethyl α-bromoisobutyrate, to yield the hydroxy-ester (VI; R = H, R′ = Et, R″ = Me) which was dehydrated to the hex-3-ene (VII; R = H, R′ = Et, R″ = Me) by potassium hydrogen sulphate. 3-*p*-Methoxyphenylpropionaldehyde similarly yielded the hydroxy-ester (VI; R = R′ = R″ = H), but neither phosphorus oxychloride nor potassium hydrogen sulphate brought about the required dehydration.

A different approach to the synthesis of branched-chain acids related to doisynolic acid used malonic ester. 3-Chloromethyl- and 3-bromomethyl-2-*p*-methoxyphenylpentane (XIV; X = Cl and Br) were obtained from the alcohol (XIV; X = OH) by thionyl chloride and phosphorus tribromide respectively, and the chloride was converted into the iodide. The bromide and, better, the iodide with diethyl sodiomethylmalonate gave the diester (XV), whence hydrolysis gave a crystalline dicarboxylic acid in 57% yield. This decomposed at *ca.* 140° to the oily monocarboxylic acid (XVI; R = H), characterised as its ethyl ester.

The branched-chain hydroxy-esters (VI; R = R′ = R″ = H; and R = H, R′ = Et, R″ = Me), the unsaturated esters (X and VII, R = Me, R′ = Et, R″ = H; and VII, R = H, R′ = Et, R″ = Me), the malonate (XV), and the saturated ester (XVI; R = Et) were examined for œstrogenic activity on ovariectomized mice. The hydroxy-esters and the malonate were inactive at a dose of 5 mg. The most active compound was the saturated ester (XVI; R = Et) which was *ca.* 600 times less active than diethylstilbœstrol, *i.e.*, approximately equal in potency to the previously reported ester (II). Even after allowance for the fact that the compounds tested are mixtures of stereoisomers, it appears that further chain-branching in compounds of this type has no marked effect on œstrogenic potency.

Details of the biological tests will be reported elsewhere.

[7] Evans, *J.*, 1956, 4691.
[8] Brown and McFarlin, *J. Amer. Chem. Soc.*, 1956, **78**, 252.
[9] *Idem*, *ibid.*, 1958, **80**, 5372; Brown and Subba Rao, *ibid.*, p. 5377.

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Experimental

Infrared spectra were determined on liquid films unless stated otherwise.

Reaction of Grignard Reagents with α-Ethyl-p-methoxystyryl Methyl Ketone.—(a) *Methylmagnesium bromide.* α-Ethyl-*p*-methoxystyryl methyl ketone (10·2 g.) in dry ether (30 c.c.) was added slowly with stirring to ethereal methylmagnesium bromide, made from magnesium (3·63 g.), cooled in ice–salt. Stirring was continued for a further 2 hr. and the solution poured into ice and concentrated hydrochloric acid. The ethereal layer was separated, the aqueous layer was further extracted with ether, and the combined ethereal solutions were washed and dried ($MgSO_4$). Distillation yielded *2-ethyl-1-p-methoxyphenyl-3-methylbutadiene* (7·4 g.), b. p. 96—97°/0·1 mm., $\lambda_{max.}$ 219 (ε 10,000), 275 mμ (ε 13,700) (Found: C, 83·4; H, 9·0. $C_{14}H_{18}O$ requires C, 83·2; H, 8·9%).

(b) *Methylmagnesium iodide in the presence of cuprous chloride.* Methylmagnesium iodide was prepared from magnesium (3·63 g.) and methyl iodide (21·5 g.) in dry ether (150 c.c.). Cuprous chloride (0·15 g.) was added, the solution cooled in ice–salt, and α-ethyl-*p*-methoxystyryl methyl ketone (12·75 g.) added during 30 min. The mixture was stirred for a further hr., left at room temperature overnight, then heated under reflux for 1 hr. Working up in the usual manner gave *3-ethyl-4-p-methoxyphenylpentan-2-one* (1·6 g.), b. p. 102—104°/0·2 mm. (Found: C, 76·3; H, 8·9. $C_{14}H_{20}O_2$ requires C, 76·3; H, 9·1%). It yielded a *semicarbazone*, m. p. 167—168° (Found: C, 64·9; H, 8·2; N, 15·3. $C_{12}H_{23}O_2N_3$ requires C, 64·95; H, 8·3; N, 15·2%).

(c) *Ethylmagnesium bromide.* The ketone (71 g.) was treated with ethylmagnesium bromide, prepared from magnesium (25·3 g.) and ethyl bromide (125 g.), as described in (*a*). Distillation of the product yielded an oil (67·6 g.), b. p. 114—116°/0·2 mm. It rapidly decolorised permanganate in the cold and had $\nu_{max.}$ 1709s (saturated C=O), no absorption at 1667 cm.$^{-1}$ (absence of C·C·C=O), $\lambda_{max.}$ 225 ($E^{1\%}_{1\,cm.}$ 417) and 277 mμ ($E^{1\%}_{1\,cm.}$ 393) in ethanol. On microhydrogenation (Pd–C) 39·1 mg. absorbed 3·16 c.c., equivalent to 35·7% of 2-ethyl-1-*p*-methoxyphenyl-3-methylpenta-1,3-diene.

3-4′-Methoxybenzylpentan-2-one.—α-Ethyl-*p*-methoxystyryl methyl ketone (50 g.) in 95% alcohol (100 c.c.) was hydrogenated at atmospheric pressure in presence of 5% palladium–charcoal (1 g.). When the hydrogen uptake (7·5 l.) was complete, the catalyst was filtered off, the alcohol evaporated, and the residue in benzene (250 c.c.) added, with stirring, to a solution of sodium dichromate (34 g.) in acetic acid (25 c.c.), concentrated sulphuric acid (45 c.c.), and water (150 c.c.). Stirring was continued for 6 hr. at 25—30°. The benzene layer was separated and washed with water, dilute sodium hydroxide, and water. Distillation of the dried ($MgSO_4$) benzene solution gave *3-4′-methoxybenzylpentan-2-one* (12·5 g.), b. p. 80—83°/0·1 mm. (Found: C, 76·0; H, 8·8. $C_{13}H_{18}O_2$ requires C, 75·75; H, 8·7%), $\nu_{max.}$ 1712s cm.$^{-1}$.

An attempt to obtain 3-4′-methoxybenzylpentan-2-one by controlled hydrogenation of the styryl ketone with palladium–charcoal resulted in a mixture of the saturated ketone, unreduced starting material, and alcohol.

Ethyl 4-4′-Methoxybenzyl-3-methylhex-2-ene-2-carboxylate.—3-4′-Methoxybenzylpentan-2-one (10·2 g.) was mixed with ethyl α-bromopropionate (8·1 g.) and dry benzene (20 c.c.), and a little of the mixture (5 c.c.) added to zinc (3·5 g.). A trace of mercuric chloride was added and the mixture heated until reaction commenced. The remainder of the ketone–bromo-ester mixture was then added during 30 min. The mixture was stirred and heated under reflux for a further 2 hr. The cooled mixture was poured into ice-cold 20% sulphuric acid (40 c.c.), the benzene layer separated, and the aqueous layer extracted with benzene. The combined benzene solutions were washed with 5% sulphuric acid, 10% sodium carbonate solution, and water. Distillation of the dried ($MgSO_4$) benzene solution gave a mixture (4·15 g.), b. p. 138—144°/0·2 mm., of ethyl 3-hydroxy-4-4′-methoxybenzyl-3-methylhexane-2-carboxylate and 4-4′-methoxybenzyl-3-methylhex-2-ene-2-carboxylate.

The mixture (4·15 g.) was heated with iodine (0·07 g.) on the steam-bath for 30 min., and the product dissolved in ether and washed with thiosulphate solution. Distillation of the dried ($MgSO_4$) ethereal solution gave two fractions, b. p. 118—120°/0·05 mm. and 124—126°/0·05 mm., both of which were mixtures of the hydroxy- and the unsaturated ester, $\nu_{max.}$ 3571m, 1739 sh, 1718s cm.$^{-1}$.

The combined fractions (2·4 g.) were heated at 190—200° for 15 min. with anhydrous potassium hydrogen sulphate (2·5 g.) in an atmosphere of nitrogen. The cooled material was

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extracted with ether, and the ethereal solution distilled, yielding *ethyl* 4-4′-*methoxybenzyl*-3-*methylhex*-2-*ene*-2-*carboxylate* (1·62 g.), b. p. 116—120°/0·1 mm. (Found: C, 74·55; H, 8·65. $C_{16}H_{26}O_3$ requires C, 74·5; H, 9·0%), $\nu_{max.}$ 1730s, no band at 3571 or 1739 cm.$^{-1}$, $\lambda_{max.}$ 225 (ε 11,700), 278 (ε 4720), and 284 mμ (ε 4450) in ethanol.

Ethyl-4-4′-*Methoxybenzyl*-2,3-*dimethylhex*-3-*ene*-2-*carboxylate*.—3-4′-Methoxybenzylpentan-2-one (39·6 g.) was treated with zinc (13·5 g.) and ethyl α-bromoisobutyrate (37·5 g.) in dry benzene (40 c.c.) in the usual way. The crude product (35·2 g.) was heated with anhydrous potassium hydrogen sulphate (20 g.) at 180° for 15 min., the mixture extracted with ether, and the ethereal solution distilled, to yield *ethyl* 4-4′-*methoxybenzyl*-2,3-*dimethylhex*-3-*ene*-2-*carboxylate* (4·87 g.), b. p. 124—126°/0·05 mm. (Found: C, 75·0; H, 8·85. $C_{19}H_{28}O_3$ requires C, 75·0; H, 9·2%), $\nu_{max.}$ 1736s cm.$^{-1}$, $\lambda_{max.}$ 225 (ε 13,180), 278 (ε 5470), and 284 mμ (ε 4970) in ethanol.

Use of magnesium in place of zinc did not give the required product.

4-p-*Methoxyphenylhexan*-3-*ol*.—4-*p*-Methoxyphenylhexan-3-one [6] (36·3 g.) in dry ether (50 c.c.) was added gradually with stirring, at room temperature, to lithium aluminium hydride (1·9 g.) in ether (100 c.c.), then stirred and heated on a water-bath for 1 hr. The excess of hydride was decomposed by water, and the precipitate filtered off. The ethereal filtrate and the ether-washings of the precipitate were combined, dried ($MgSO_4$), and evaporated. Distillation of the residue gave 4-*p*-methoxyphenylhexan-3-ol (33·1 g.), b. p. 107—109°/0·5 mm. (Found: C, 75·05; H, 9·3. Calc. for $C_{13}H_{20}O_2$: C, 75·0; H, 9·6%). Rubin,[10] by using sodium and isopentyl alcohol, obtained a crystalline isomer, b. p. 100—105°/0·2 mm., m. p. 75—76°.

2-p-*Methoxyphenylpentan*-3-*one*.—Methyl iodide (191·5 g.) was added, with cooling and stirring, in 3 min., to a mixture of ethyl *p*-methoxybenzyl ketone [6] (80·0 g.) and sodium methoxide (48·5 g.) under nitrogen. After the initial reaction had subsided, the stirring was continued and the mixture heated on a steam-bath under a reflux condenser, further small quantities of methyl iodide being added if the mixture became too viscous. After 1 hr. the surplus methyl iodide was distilled off, water (200 c.c.) added, and the oil extracted with ether. The ethereal extract was washed with sodium thiosulphate solution and water, and dried ($MgSO_4$). Distillation yielded 2-*p*-methoxyphenylpentan-3-one (71·3 g.), b. p. 96°/0·4 mm.

2-p-*Methoxyphenylpentan*-3-*ol*.—2-*p*-Methoxyphenylpentan-3-one (71 g.), reduced with lithium aluminium hydride (4·0 g.) as described for the hexanone, gave 2-p-*methoxyphenylpentan*-3-*ol* (66·5 g.), b. p. 104—106°/0·5 mm. (Found: C, 74·1; H, 9·4. $C_{12}H_{18}O_2$ requires C, 74·2; H, 9·3%).

3-*Bromo*-4-p-*methoxyphenylhexane*.—4-*p*-Methoxyphenylhexan-3-ol (36 g.) in carbon tetrachloride (50 c.c.) was cooled in an ice-bath, and phosphorus tribromide (17 g.) added gradually to the stirred solution. The mixture was stirred at room temperature for 2 days and then on a steam-bath for 1 hr. The solution was washed with water and then dried ($MgSO_4$). Distillation yielded 3-bromo-4-*p*-methoxyphenylhexane (36·4 g.), b. p. 114—116°/0·5 mm. (Found: Br, 29·1. Calc. for $C_{13}H_{19}OBr$: Br, 29·5%).

3-*Chloro*-2-p-*methoxyphenylpentane*.—2-*p*-Methoxyphenylpentan-3-ol (66 g.) in dry benzene (100 c.c.) was added, during 30 min., at room temperature, to a stirred solution of thionyl chloride (48·2 g.) in benzene (50 c.c.) containing one drop of pyridine. The mixture was heated on the steam-bath for 1 hr., cooled, and poured into iced water. The benzene layer was separated, washed successively with water, sodium hydrogen carbonate solution, and water, and dried ($CaCl_2$). Distillation yielded 3-*chloro*-2-p-*methoxyphenylpentane* (64·8 g.), b. p. 95—97°/0·5 mm. (Found: C, 67·6; H, 8·1; Cl 16·9. $C_{12}H_{17}OCl$ requires C, 67·8; H, 8·0; Cl 16·7%).

Reaction Between Ethyl Orthoformate and 1-*Ethyl*-2-p-*methoxyphenylpropylmagnesium Chloride*.—Ethyl orthoformate (19·6 g.) was added slowly to a solution, at −10°, of the Grignard reagent from 3-chloro-2-*p*-methoxyphenylpentane (34 g.) and magnesium (3·9 g.), in dry ether (100 c.c.). A crystal of iodine was needed to start the formation of the Grignard reagent. The mixture was stirred and heated on a water-bath for 6 hr., allowed to cool, and decomposed with ice and ammonium chloride. The aqueous layer was extracted with ether. The oily residue, from the distillation of the combined ether solutions, was boiled with 5N-hydrochloric acid (100 c.c.) for 1 hr., cooled, and extracted with ether. The ethereal extracts were washed with water, sodium hydrogen carbonate solution, and water, and dried ($MgSO_4$). Distillation gave, in addition to recovered ethyl orthoformate and chloride (13·3 g.), an oil (3·9 g.), b. p. 76—88°/0·6 mm. On reaction with 2,4-dinitrophenylhydrazine sulphate in alcohol this yielded 2-*ethyl*-3-p-*methoxyphenylbutyraldehyde* 2,4-*dinitrophenylhydrazone* (0·4 g.), m. p. 146—147° (Found:

[10] Rubin, *J. Amer. Chem. Soc.*, 1944, **66**, 2075.

C, 59·25; H, 5·85; N, 14·7. $C_{19}H_{22}O_5N_4$ requires C, 59·1; H, 5·7; N, 14·5%), $\lambda_{max.}$ 357 mμ (ε 26,600) in ethanol.

4-Methoxyphenethyl Alcohol.—(*a*) Reduction of ethyl *p*-methoxyphenylacetate (40 g.) in dry ether with lithium aluminium hydride (5 g.) in the usual manner gave 4-methoxyphenethyl alcohol (27·8 g.), b. p. 142°/12 mm., m. p. 23° (Shoesmith and Connor,[11] m. p. 24°).

Reduction of the free carboxylic acid was less successful, resulting in only a 50% yield.

(*b*) The alcohol was also obtained by a modification of the method of Plimmer, Short, and Hill,[12] whereby the duration of the reaction was considerably reduced. Ethylene oxide (32·2 g.) in ether (50 c.c.), cooled in ice–salt, was added slowly to cold ethereal *p*-methoxyphenylmagnesium bromide, prepared from *p*-bromoanisole (152 g.) and magnesium (19·5 g.). The mixture was then stirred and heated under reflux for 1 hr., dry benzene (300 c.c.) added, and the ether distilled. The resulting benzene solution was heated under reflux for 4 hr., then cooled, and a saturated solution of ammonium chloride added. The benzene layer was separated and the aqueous layer extracted with benzene. The combined benzene solutions were dried (Na_2SO_4) and distilled, yielding 4-methoxyphenethyl alcohol (63 g.), b. p. 138—140°/10 mm.

4-Methoxyphenethyl Chloride.—4-Methoxyphenethyl alcohol (27·8 g.) in dry benzene (150 c.c.) was added during 1 hr., with stirring at room temperature, to thionyl chloride (25·8 g.) in benzene (100 c.c.) containing pyridine (0·2 c.c.). The mixture was heated on a water-bath for 1 hr. cooled, and poured into iced water. The oil was extracted into benzene, and the benzene solution washed with water, sodium hydrogen carbonate solution, and water. The dried ($CaCl_2$) benzene solution was distilled, yielding 4-methoxyphenethyl chloride (19·3 g.), b. p. 116—120°/8 mm. (lit.,[12] b. p. 100—105°/7 mm.).

3-p-Methoxyphenylpropionaldehyde.—Ethyl orthoformate (13·8 g.) was caused to react with 4-methoxyphenethylmagnesium chloride prepared from 4-methoxyphenethyl chloride (19·3 g.) and magnesium (2·75 g.) in dry ether (100 c.c.), and the product hydrolysed as described for the homologue. The aldehyde (5·0 g.), b. p. 140°/12 mm., was obtained (Found: C, 71·7; H, 7·25. Calc. for $C_{10}H_{12}O_2$: C, 73·2; H, 7.32%), having $\nu_{max.}$ 2740w and 1727s cm.$^{-1}$.

Ethyl α-Ethyl-β-hydroxy-β-p-methoxyphenylbutyrate.—4-Methoxyacetophenone (220 g.), ethyl α-bromobutyrate (286 g.), and dry benzene (300 c.c.) were mixed and a portion of the mixture (20 c.c.) added with stirring and heating under reflux, to zinc (110 g.) with a trace of mercuric chloride. When the reaction started, the remainder of the mixture was added gradually, and stirring and heating were continued for a further 2 hr. The cooled mixture was poured into 20% ice-cold sulphuric acid, the benzene layer separated, and the aqueous layer extracted with benzene. The combined benzene solutions were washed successively with water, dilute sodium carbonate solution, and water, and dried ($MgSO_4$). Distillation yielded the *hydroxy-ester* (105 g.), b. p. 132—134°/0·5 mm. (Found: C, 68·4; H, 8·35. $C_{15}H_{22}O_4$ requires C, 67·7; H, 8·3%).

Dehydration of Ethyl α-Ethyl-β-hydroxy-β-p-methoxyphenylbutyrate.—(*a*) The hydroxy-ester (105 g.) was heated on a steam-bath for 2 hr. with iodine (1·5 g.), dissolved in ether, washed with sodium thiosulphate solution and water, and dried ($MgSO_4$). Distillation yielded *ethyl 2-ethyl-3-p-methoxyphenylbut-2-enoate* (89 g.), b. p. 126—128°/0·5 mm. (Found: C, 72·4; H, 8·25. $C_{15}H_{20}O_3$ requires C, 72·6; H, 8·1%), $\nu_{max.}$ 1730s cm.$^{-1}$.

(*b*) The dried benzene solution from the reaction between 4-methoxyacetophenone (267 g.), ethyl α-bromobutyrate (347 g.), and zinc (139 g.) was not distilled but heated under reflux with phosphorus oxychloride (12 c.c.) for 1·5 hr. The cooled solution was washed successively with water, sodium hydrogen carbonate solution, and water, dried ($MgSO_4$), and distilled. After distillation of unchanged ketone, a fraction of b. p. 124—134°/0·5 mm., containing only a little ketone, was obtained. Redistillation of this fraction through a column packed with Dixon gauze rings yielded the butenoate (160·5 g.), b. p. 132—134°/0·6 mm.

α-Ethyl-β-p-methoxyphenylbutyric Acid.—The above ester (40 g.) was heated under reflux with 20% alcoholic potassium hydroxide (150 c.c.) for 3 hr. Water (200 c.c.) was added, the mixture acidified to Congo Red, cooled, and extracted with ether. The residue, after evaporation of the ether, was dissolved in 10% aqueous sodium hydroxide (1 l.). The solution was heated at 90° and nickel–aluminium alloy (130 g.) added gradually with stirring. When this addition was complete, a further 150 c.c. of sodium hydroxide solution and 15 g. of alloy were added. The hot liquid was filtered under reduced pressure, and the precipitate washed

[11] Shoesmith and Connor, *J.*, 1927, 2230.
[12] Plimmer, Short, and Hill, *J.*, 1938, 694.

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with hot water. The cooled filtrate was poured slowly, with vigorous stirring, into concentrated hydrochloric acid (500 c.c.). The organic acid was extracted from the co-precipitated sodium chloride with ether. Distillation of the ether left a sticky brown solid which recrystallised from 33% aqueous acetic acid and then from light petroleum (b. p. 80—100°), yielding needles of *α-ethyl-β-p-methoxyphenylbutyric acid* (10 g.), m. p. 81—82° (Found: C, 70·6; H, 8·1. $C_{13}H_{18}O_3$ requires C, 70·3; H, 8·1%), $\nu_{max.}$ (in Nujol mull) 1704s cm.$^{-1}$.

α-Ethyl-β-p-methoxyphenylbutyryl Chloride.—The above acid (7·1 g.) and thionyl chloride (8·1 g.) were kept at 60° for 10 hr. Distillation yielded the *acid chloride* (6·7 g.), b. p. 116—117°/0·5 mm. (Found: C, 65·1; H, 7·1. $C_{13}H_{17}O_2Cl$ requires C, 64·9, H, 7·1%).

2-Ethyl-3-p-methoxyphenylbut-2-en-1-ol.—Ethyl 2-ethyl-3-*p*-methoxyphenylbut-2-enoate (40 g.) was reduced with lithium aluminium hydride (3·5 g.) in ether (150 c.c.) to *2-ethyl-3-p-methoxyphenylbut-2-en-1-ol* (29·5 g.), b. p. 123—126°/0·5 mm. (Found: C, 75·15; H, 8·7. $C_{13}H_{18}O_2$ requires C, 75·7; H, 8·7%).

Oxidation of 2-Ethyl-3-p-methoxyphenylbut-2-en-1-ol with Manganese Dioxide.—The alcohol (12·5 g.) in dry light petroleum (b. p. 60—80°; 300 c.c.) was stirred with freshly prepared manganese dioxide (30 g.), at room temperature for 5 days. The mixture was filtered, the precipitate washed with light petroleum, and the filtrate distilled, yielding, besides recovered alcohol (9·5 g.), a fraction (2·7 g.) of b. p. 112—120°/0·5 mm., shown by its infrared spectrum to be a mixture of unchanged alcohol and the αβ-unsaturated aldehyde ($\nu_{max.}$ 1672 cm.$^{-1}$). An attempt to isolate the aldehyde as its bisulphite compound was unsuccessful, but the mixture yielded *2-ethyl-3-p-methoxyphenylbutyraldehyde 2,4-dinitrophenylhydrazone*, m. p. 176—177° (Found: C, 58·8; H, 5·25; N, 14·6. $C_{19}H_{20}O_5N_4$ requires C, 59·4; H, 5·2; N, 14·6%), $\lambda_{max.}$ 396 mμ (ε 29,200) in ethanol.

Ethyl α-Ethyl-β-p-methoxyphenylbutyrate.—Ethyl 2-ethyl-3-*p*-methoxyphenylbut-2-enoate (89 g.) in 95% alcohol (100 c.c.) was heated on a steam-bath for 4 hr. with Raney nickel to remove sulphur-containing impurities. The Raney nickel was filtered off and the alcoholic solution of the ester shaken with platinum oxide (0·2 g.) and hydrogen at atmospheric pressure. Three days were required for the theoretical uptake of hydrogen, and fresh platinum oxide (0·1 g.) was added as required. The catalyst was filtered off and the filtrate distilled, yielding *ethyl α-ethyl-β-p-methoxyphenylbutyrate* (75 g.), b. p. 111—112°/0·2 mm. (Found: C, 72·4; H, 8·4. $C_{15}H_{22}O_3$ requires C, 72·0; H, 8·8%), $\nu_{max.}$ 1733s cm.$^{-1}$, $\lambda_{max.}$ 224·5 (ε 15,580), 275 mμ (ε 3160) in ethanol.

2-Ethyl-3-p-methoxyphenylbutan-1-ol.—(*a*) The foregoing ester (75 g.) was reduced in ether with lithium aluminium hydride (6·5 g.), giving *2-ethyl-3-p-methoxyphenylbutan-1-ol* (53 g.), b. p. 120—122°/0·4 mm. (Found: C, 75·15; H, 9·45. $C_{13}H_{20}O_2$ requires C, 75·0; H, 9·6%), $\nu_{max.}$ 3333s cm.$^{-1}$. (*b*) 2-Ethyl-3-*p*-methoxyphenylbut-2-en-1-ol (36·3 g.) was hydrogenated at atmospheric pressure and temperature, in alcohol (100 c.c.), with 5% palladium–charcoal (1 g.). Hydrogen uptake was complete in 3 hr. Isolation in the usual way gave the saturated alcohol (29·4 g.), b. p. 124—126°/0·6 mm.

2-Ethyl-3-p-methoxyphenylbutyraldehyde.—Chromic anhydride (40·5 g.) in dry pyridine (400 c.c.) was added to a solution of the butyl alcohol (29·4 g.) in pyridine (400 c.c.). The mixture was shaken and left in a stoppered vessel overnight at room temperature, then poured into water (2 l.), and the solid material was filtered off through "Hyflo super-cel." The filtrate was extracted with ether, and the ether extract dried ($MgSO_4$). Distillation, and redistillation through an efficient column, yielded the *aldehyde* (10·6 g.), b. p. 109—110°/0·5 mm. (Found: C, 75·05; H, 8·7. $C_{13}H_{18}O_2$ requires C, 75·7; H, 8·7%), $\nu_{max.}$ 2732w and 1730s cm.$^{-1}$ (2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 146°).

Ethyl 4-Ethyl-3-hydroxy-5-p-methoxyphenyl-2-methylhexane-2-carboxylate.—The preceding aldehyde (10·6 g.), ethyl α-bromoisobutyrate (8·2 g.), and zinc (4·0 g.) amalgamated with a trace of mercuric chloride, were caused to react together in dry benzene (30 c.c.) in the usual way. Decomposition of the resulting complex with ice-cold 20% sulphuric acid (40 c.c.), extraction with benzene, and distillation of the benzene solution yielded *ethyl 4-ethyl-3-hydroxy-5-p-methoxyphenyl-2-methylhexane-2-carboxylate* (8·5 g.), b. p. 162—164°/0·5 mm. (Found: C, 71·1; H, 9·2. $C_{19}H_{30}O_4$ requires C, 70·8; H, 9·3%), $\nu_{max.}$ 3650m and 1736s cm.$^{-1}$.

Ethyl 4-Ethyl-5-p-methoxyphenyl-2-methylhex-3-ene-2-carboxylate.—Ethyl 4-ethyl-3-hydroxy-5-*p*-methoxyphenyl-2-methylhexane-2-carboxylate (6·0 g.) was heated with anhydrous potassium hydrogen sulphate (6 g.) for 30 min. at 190°. The organic material was extracted from the cooled mixture with ether and distilled, yielding fractions, b. p. 130—142°/0·5 mm.

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(1·1 g.), 146—156°/0·5 mm. (1·0 g.), and 162—164°/0·5 mm. (3·3 g.), each of which was shown to contain a hydroxyl group by infrared analysis.

Two further treatments with potassium hydrogen sulphate yielded *ethyl* 4-*ethyl*-5-p-*methoxyphenyl*-2-*methylhex*-3-*ene*-2-*carboxylate* (0·7 g.), b. p. 135—145°/0·9 mm. (Found: C, 74·9; H, 9·1. $C_{19}H_{28}O_3$ requires C, 75·0; H, 9·2%), $\nu_{max.}$ 1733s cm.$^{-1}$.

Ethyl 3-*Hydroxy*-5-p-*methoxyphenyl*-2-*methylpentane*-2-*carboxylate and its Attempted Dehydration.*—3-*p*-Methoxyphenylpropionaldehyde (5 g.), ethyl α-bromoisobutyrate (5·95 g.), and zinc (3 g.) with a trace of mercuric chloride, reacted in benzene (40 c.c.) in the usual way. The complex was decomposed with ice-cold 20% sulphuric acid (40 c.c.), and the organic material taken into benzene. The benzene solution was dried ($MgSO_4$), and then heated under reflux for 1·5 hr. with phosphorus oxychloride (1·0 c.c.). The cooled product was washed with water and sodium hydrogen carbonate solution, and dried ($MgSO_4$). Distillation yielded *ethyl* 3-*hydroxy*-5-p-*methoxyphenyl*-2-*methylpentane*-2-*carboxylate* (2·5 g.), b. p. 152—154°/0·5 mm. (Found: C, 68·5; H, 8·5. $C_{16}H_{24}O_4$ requires C, 68·6; H, 8·75%), $\nu_{max.}$ 3560m, and 1724s cm.$^{-1}$. The low value for the carbonyl band is anomalous. The analytical figures preclude the material's being a mixture of hydroxy- and unsaturated ester.

Heating this hydroxy-ester (2·5 g.) with potassium hydrogen sulphate (2 g.) at 190° for 30 min. did not yield the unsaturated ester.

2-*Ethyl*-3-p-*methoxyphenylbutyl Bromide.*—Phosphorus tribromide (10 g.) was added gradually to a stirred solution of 2-ethyl-3-*p*-methoxyphenylbutan-1-ol (20 g.) in carbon tetrachloride (50 c.c.) at 0°. The mixture was left at room temperature for 5 days, then heated under a reflux for 1 hr., cooled, washed with water, and dried ($MgSO_4$). Distillation yielded the *bromide* (8·5 g.), b. p. 124—126°/0·5 mm. (Found: C, 59·3; H, 7·25; Br, 29·45. $C_{13}H_{19}OBr$ requires C, 57·6; H, 7·0; Br, 29·5%).

2-*Ethyl*-3-p-*methoxyphenylbutyl Chloride.*—2-Ethyl-3-*p*-methoxyphenylbutan-1-ol (20 g.) in dry benzene (100 c.c.) was added, at room temperature, during 30 min., to thionyl chloride (13·6 g.) in benzene (50 c.c.) containing one drop of pyridine. The mixture was heated on a steam-bath for 1 hr., allowed to cool, and poured into iced-water, the benzene layer was separated, and the aqueous layer was extracted with benzene. The combined benzene solutions were washed with water and sodium hydrogen carbonate solution and dried ($CaCl_2$). Distillation yielded the *chloride* (15·6 g.), b. p. 116—118°/0·7 mm. (Found: C, 68·5; H, 8·2. $C_{13}H_{19}OCl$ requires C, 68·9; H, 8·4%).

Diethyl 4-*Ethyl*-5-p-*methoxyphenylhexane*-2,2-*dicarboxylate.*—(*a*) Diethyl methylmalonate (4·9 g.) was added to a stirred solution, at 50—60°, of sodium ethoxide, prepared from sodium (0·61 g.) and dry ethanol (7·2 c.c.). The temperature was allowed to fall to *ca.* 35°, then 2-ethyl-3-*p*-methoxyphenylbutyl bromide (7·5 g.) was added, and the mixture was stirred overnight. The alcohol was distilled from the neutral mixture, water (10 c.c.) added, and the mixture acidified with acetic acid. Extraction with benzene and distillation of the dried ($MgSO_4$) extract yielded *diethyl* 4-*ethyl*-5-p-*methoxyphenylhexane*-2,2-*dicarboxylate* (4·7 g.), b. p. 166—168°/0·2 mm. (Found: C, 68·95; H, 8·6. $C_{21}H_{32}O_5$ requires C, 69·2; H, 8·8%).

(*b*) 2-Ethyl-3-*p*-methoxyphenylbutyl chloride (14 g.) was stirred and heated overnight with dry sodium iodide (11·3 g.) in dry acetone (100 c.c.). The acetone was distilled and the precipitate filtered off and washed with ether. The ether washings were added to the filtrate, and this ethereal solution was washed with sodium thiosulphate solution and water and dried ($MgSO_4$). Distillation yielded the iodide (11·2 g.), b. p. 122—126°/0·6 mm.

This iodide (9·4 g.) was added to an alcoholic solution of diethyl sodiomethylmalonate, prepared from sodium (0·65 g.), ethanol (10 c.c.), and diethyl methylmalonate (5·2 g.) as described above. On working up in the usual manner, diethyl 4-ethyl-5-*p*-methoxyphenylhexane-2,2-dicarboxylate (5·3 g.), b. p. 169—172°/0·5 mm., was obtained.

4-*Ethyl*-5-p-*methoxyphenylhexane*-2,2-*dicarboxylic Acid.*—The diethyl ester (4·6 g.) was heated under reflux for 4 hr. with 2N-alcoholic potassium hydroxide (50 c.c.). The cooled solution was diluted with water (150 c.c.) and acidified with hydrochloric acid. The brown viscous oil which separated was added to boiling light petroleum (b. p. 60—80°), in which it is only slightly soluble, and ethylene dichloride added to complete the dissolution. The solid white precipitate formed on cooling was recrystallised from 30% aqueous methanol, to yield 4-*ethyl*-5-p-*methoxyphenylhexane*-2,2-*dicarboxylic acid* (2·2 g.) (Found: C, 66·35; H, 7·6. $C_{17}H_{24}O_5$ requires C, 66·3; H, 7·8%).

Ethyl 4-*Ethyl*-5-p-*methoxyphenylhexane*-2-*carboxylate.*—The above dicarboxylic acid (2·1 g.)

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was heated at 160° in nitrogen until the evolution of carbon dioxide ceased. The crude monocarboxylic acid (1·6 g.) did not crystallise.

Esterification by the Fischer–Spier method yielded *ethyl 4-ethyl-5-p-methoxyphenylhexane-2-carboxylate* (0·8 g.), b. p. 135—138°/0·5 mm. (Found: C, 74·1; H, 9·6. $C_{18}H_{28}O_3$ requires C, 74·0; H, 9·6%).

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754. *Complex Fluorides. Part XII.* The Structures of Some Complex Acid Fluorides.*

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Three compounds of the formula type $M^{I}_3HM^{IV}F_8$ have been studied by *X*-ray powder photography and infrared spectroscopy, and the results are considered in relation to early morphological work, a single-crystal *X*-ray study of K_3HNbOF_7, and the infrared spectrum of potassium hydrogen difluoride. In the solid state these compounds are composed of M^{I+}, $M^{IV}F_6^{2-}$, and HF_2^- ions: K_3HSnF_8 and K_3HPbF_8 are isostructural with monoclinic K_3HNbOF_7, but Na_3HTiF_8 has a different (orthorhombic) structure.

HOARD and MARTIN'S demonstration,[1] by *X*-ray crystallography, that the compound K_3HNbOF_7 is a lattice aggregate of K^+, HF_2^-, and $NbOF_5^{2-}$ ions is the only detailed investigation of the structure of a complex acid fluoride yet reported. The present paper concerns the somewhat similar compounds K_3HPbF_8, K_3HTiF_8, and Na_3HTiF_8; in addition to *X*-ray powder photography, however, infrared spectroscopy has been used to show the presence of HF_2^- ions, and the spectra have been considered in some detail. Early morphological studies [2] of these compounds showed that the two potassium salts have axial ratios very close to those [1,3] of the compound K_3HNbOF_7, and it has been found that their powder photographs can be indexed on the basis of monoclinic unit cells having dimensions similar to those given by Hoard and Martin for the niobium compound (Table 1). The compound Na_3HTiF_8 has an orthorhombic unit cell whose dimensions are closely related to the monoclinic unit cells of K_3HPbF_8, K_3HSnF_8, and K_3HNbOF_7; β is 90° instead of 86—87°, and the *a*-side is shortened. Since the $NbOF_5^{2-}$, PbF_6^{2-}, SnF_6^{2-}, and TiF_6^{2-} ions are all octahedral and almost isodimensional, these results provide strong evidence for the presence of HF_2^- ions in the compounds which have now been investigated. This conclusion is supported by a comparison of the infrared absorption bands of the compounds in Table 2, in which frequencies previously shown [4-7] to be associated with the

TABLE 1. *X-Ray and morphological crystallographic data.*

Compound	Morphological axial ratios, β	Unit-cell dimensions (Å) *a*	*b*	*c*	β	Axial ratios	*Z*	Density Calc.	Found
K_3HNbOF_7	0·630 : 1 : 0·489 [3] β = 86° 41′	8·82	14·02	6·82	86° 34′	0·629 : 1 : 0·486 [1]	4	2·72	2·68
K_3HPbF_8 ...	0·622 : 1 : 0·482 [2] β = 86° 41′	8·93	14·38	6·93	85° 59′	0·622 : 1 : 0·485	4	3·57	3·51
K_3HSnF_8 ...	0·628 : 1 : 0·493 [2] β = 87° 0′	8·84	14·08	6·83	86° 25′	0·628 : 1 : 0·482	4	3·05	3·00
Na_3HTiF_8	0·517 : 1 : 0·466 [2] β = 90°	7·17	13·96	6·54	90°	0·514 : 1 : 0·469	4	2·73	2·68

* Part XI, *J.*, 1957, 4804.

[1] Hoard and Martin, *J. Amer. Chem. Soc.*, 1941, **63**, 11.
[2] Groth, "Chemische Krystallographie," Vol. I, Engelmann, Leipzig, 1906, pp. 463—464.
[3] Balke and Smith, *J. Amer. Chem. Soc.*, 1908, **30**, 1637.
[4] Coté and Thompson, *Proc. Roy. Soc.*, 1951, *A*, **210**, 206.
[5] Ketelaar and Vedder, *J. Chem. Phys.*, 1951, **19**, 654.
[6] Newman and Badger, *ibid.*, 1951, **19**, 1207.
[7] Ketelaar, Haas, and van der Elsken, *ibid.*, 1956, **24**, 624.

HF_2^- ion are listed in the left-hand column, while those observed in this work are denoted by the letter *A* in the right-hand column.

The linear ion HF_2^- has three fundamental frequencies: ν_1 (symmetrical stretching) at about 600 cm.$^{-1}$; ν_2 (doubly degenerate bending) at 1220 cm.$^{-1}$; ν_3 (antisymmetric stretching) at 1425 cm.$^{-1}$. Only ν_2 and ν_3 are infrared-active, but ν_1 appears in combination frequencies. It has recently been found [7] that the infrared spectra of ammonium, potassium, and sodium hydrogen difluorides vary with the conditions under which they are observed; in Nujol mulls the ν_3 fundamental is nearly hidden by a very broad, strong band at 1600 cm.$^{-1}$ whose half-width is about 150 cm.$^{-1}$. The spectra cited in Table 2 were observed for the finely powdered compounds with and without mulling agents.

The half-width of the ν_2 band is no more than 20 cm.$^{-1}$ at room temperature, so that it is more reliable than ν_3 for diagnostic purposes. When its double degeneracy is removed in a dissymmetric crystal lattice, the splitting of ν_2 should be resolvable as long as it exceeds 5 cm.$^{-1}$. In crystalline potassium hydrogen difluoride, the HF_2^- ions are arranged in planes perpendicular to the four-fold axis, and deformations in these planes therefore correspond to a different energy change from those at right angles. This interpretation [4] of the splitting of ν_2 in potassium hydrogen difluoride into two frequencies separated by about 20 cm.$^{-1}$ can be extended to other compounds containing this ion. It has been reported that the lattice of sodium hydrogen difluoride is rhombohedral with one molecule per unit cell; [8,9] the HF_2^- ion lies parallel to the three-fold axis, and ν_2 would therefore be expected to remain degenerate. In fact, a single frequency occurs at 1210 cm.$^{-1}$, and this has no fine structure at room temperature.

The environment of the HF_2^- ion in the monoclinic K_3HNbOF_7 lattice is more complex, but according to Hoard and Martin [1] the hydrogen atom lies at a centre of symmetry. There are six K^+ and six $NbOF_5^{2-}$ ions placed irregularly about it, as well as two HF_2^- ions. The energy of the bending vibration was estimated on a simple electrostatic model,

TABLE 2. *Infrared frequencies (cm.$^{-1}$) observed at room temperature.*

KHF_2 (lit) [a]	Assgt.	KHF_2	$NaHF_2$	K_3HNbOF_7	K_3HPbF_8	K_3HSnF_8	Na_3HTiF_8	R.I.[e]	E.I.[f]
3890—									
3660 [b]									
3240 w	$3\nu_1 + \nu_3$								
2670 ms	$2\nu_1 + \nu_3$	2660						vw	*A*
2420 w	$2\nu_1 + \nu_3$	2420						vw	*A*
2060 s	$\nu_1 + \nu_3$	2080	2120	2105	2095	2115	2090	ms	*A*
1870 s	$\nu_1 + \nu_2$	1836	1830	1830	1835	1840	1825	wm	*A*
1700 s		1600 [c]	1600 [c]	1590 [c]	1570 [c]	1600 [c]	1610 [c]	vs	*A*
1425 vs	ν_3	1460		1480 sh	1475 sh	1470 sh	1440 sh	m	*A*
—	—			1310	1310	1310		w	?
		1235 sh		1220	1232	1221	1277		
1238 }			1210				1251	s	*A*
1220 } vs	ν_2, ν'_2	1220		1183	1193	1184	1224		
		K_2TiF_6	Na_2TiF_6						
1170 vw		1020	1035	1015			1026	vw	*B*
—					965		965	w	*B*?
880 vw				918				s	*B*ii
740 vw									
		625 sh	625 sh	630 sh	509 [d]	565 [d]	630 sh		
							580	vs	*B*i
		580	563	550 [d]	490 sh	550 sh	550 sh		
		464						w	*B*?

[a] Refs. 4, 5, 6, 7, 12. [b] 3890, 3810, 3775, 3715, 3660. [c] Very broad and strong; sh = shoulder. [d] $KNbF_6$, K_2PbF_6, K_2SnF_6 absorb sharply at 580, 502, 552 cm.$^{-1}$ respectively.[10] [e] Relative intensities. [f] Excited ion; *A* hydrogen difluoride frequency; *B* octahedral ion frequency.

the ion being treated as F^-–H^+–F^-. The difference in energy for vibrations in two perpendicular planes was used to calculate the splitting of this deformation frequency as

[8] Rinne, Hentschel, and Leonhardt, *Z. Krist.*, 1923, **58**, 629.
[9] Andersen and Hassel, *Z. phys. Chem.*, 1926, **123**, 151.
[10] Peacock and Sharp, *J.*, 1959, 2762.

about 50 cm.$^{-1}$. The observed values (Table 2) show that $\Delta\nu = \nu_2 - \nu'_2$ is approximately constant at 38 ± 5 cm.$^{-1}$; ν_2 and ν'_2 have approximately equal intensities for any given compound.

The infrared spectrum of the compound Na_3HTiF_8 confirms the conclusion, from *X*-ray powder photography, that this substance is not isomorphous with K_3HNbOF_7, K_3HPbF_8, and K_3HSnF_8. The ν_2 frequency is apparently split into three components: ν_2 (1277), ν'_2 (1251), and ν''_2 (1224 cm.$^{-1}$) (all ±3 cm.$^{-1}$), with relative intensities 1 : 2 : 1, and differences $\Delta\nu$ of 26 and 27 (±5) cm.$^{-1}$. This suggests that there are two different kinds of HF_2^- ion in the lattice, giving rise to four ν_2 frequencies, two of which happen to coincide at 1251 cm.$^{-1}$.

The bands denoted by *B* in Table 2, which do not correspond to HF_2^- frequencies, and which presumably arise from the octahedral ions, may be considered in two groups, *B*(i) and *B*(ii).

B(i), at 500—630 cm.$^{-1}$, is the more complex and intense. Peacock and Sharp [10] have pointed out that frequencies in this region correspond to ν_3 for the regular MF_6^{n-} species, and that ν_4, the other infrared-active vibration, will rarely appear above 400 cm.$^{-1}$. The tin and lead compounds give rise to very similar absorptions here, the only difference being a shift of the main frequency from 565 to 509 cm.$^{-1}$, corresponding to the increase in atomic weight of the central atom. The spectra of the complex acid fluorides differ from those of $K_2M^{IV}F_6$ in that small shifts in frequency and splitting occur in the former. Thus, K_2SnF_6 and K_2PbF_6 absorb [10] quite sharply at 552 and 502 cm.$^{-1}$ respectively. These small discrepancies and splittings may be ascribed to lower symmetry and more ions in the unit cells of the complex acid fluorides. The spectrum of the $NbOF_5^{2-}$ ion has the principal band at 550 cm.$^{-1}$, whereas the fluoroanion in $KNbF_6$ absorbs [10] at 580 cm.$^{-1}$. Because the natures of the vibrations will be similar in these ions, the small shifts in frequency can be interpreted as indicating a multiple niobium–oxygen bond in the oxyfluoroanion; the addition of an electron to VF_6^-, forming VF_6^{2-}, involves [10] a shift in the absorption from 715 to 583 cm.$^{-1}$.

B(ii) is at 918 cm.$^{-1}$ in the $NbOF_5^{2-}$ spectrum. This ion will have a dipole moment, unlike the regular $M^{IV}F_6^{2-}$ ions, and this frequency will be mainly the O–NbF_5 stretching frequency as long as there is little coupling in the O–Nb(F_2F_2)–F vibration. The energy difference 918 − 550 cm.$^{-1}$ indicates that any coupling will be slight. Absorption at this frequency would then correspond to a force constant of $7{\cdot}3 \times 10^5$ dynes/cm. for the niobium–oxygen bond, which suggests a bond order higher than unity. To confirm that this frequency is due to the $NbOF_5^{2-}$ ion, the compound was partially deuterated; as a result new bands appeared corresponding to the DF_2^- spectrum, but the 918 cm.$^{-1}$ band showed no decrease in intensity and no new band was observed in the range 640—670 ($918/\sqrt{2}$) cm.$^{-1}$.

Experimental

Preparations.—Fluorotitanates were made from titanium dioxide, hydrofluoric acid, and alkali-metal carbonates by the standard methods. Titanium was determined as TiO_2; the acid salt was also analysed for hydrolysable fluoride by potentiometric titration according to the equation $Na_3HTiF_8 + 5OH^- = 3NaF + TiO_2 + 5F^- + 3H_2O$ (Found: Ti, 23·0. Calc. for Na_2TiF_6: Ti, 23·1. Found: Ti, 20·1. Calc. for K_2TiF_6: Ti, 20·0. Found: Ti, 17·7%; hydrolysable F^-, 4·95 g.-ion/mole. Calc. for Na_3HTiF_8: Ti, 17·7%; hydrolysable F^-, 5·0 g.-ion/mole).

The compound K_2HNbOF_7 was made by dissolving niobium pentoxide in 40% hydrofluoric acid and adding potassium carbonate until the solution was only slightly acidic; the product was recrystallised from dilute hydrofluoric acid (Found: Nb, 25·6. Calc. for K_2HNbOF_7: Nb, 25·8%).

Deuteration was effected by crystallisation from deuterium oxide to which a trace of the aqueous acid had been added. The compounds K_3HSnF_8 and K_3HPbF_8 were made by a modification of Mathers's method [11] for the latter compound. The dioxides were fused with

[11] Mathers, *J. Amer. Chem. Soc.*, 1920, **42**, 1309.

potassium hydrogen difluoride in a platinum dish; the difluoride was regenerated by treatment with anhydrous hydrogen fluoride and the fusion was then repeated. The process was continued until the reaction mixture contained very little unchanged oxide. The acid salts were extracted with hot 50% hydrofluoric acid, from solutions in which they crystallise on being cooled. Tin was determined as the dioxide, and lead by reduction with iodide in concentrated hydrochloric acid followed by an Andrews's titration of the excess of iodide (Found: Sn, 30·7%; hydrolysable F^-, 5·03 g.-ion/mole. Calc. for K_3HSnF_8: Sn, 30·5%; hydrolysable F^-, 5·0 g.-ion/mole. Found: Pb, 43·5%; hydrolysable F^-, 4·82 g.-ion/mole. Calc. for K_3HPbF_8: Pb, 43·4%; hydrolysable F^-, 5·0 g.-ion/mole).

Infrared Spectra.—These were measured with a Perkin-Elmer double-beam continuously-recording spectrophotometer, with sodium chloride and potassium bromide optics. The solids were examined as Nujol and hexachlorobutadiene mulls, and as fine powders between sodium chloride plates in the absence of mulling agent.

X-*Ray Powder Photographs.*—These were obtained with a 19 cm. camera and Cu-K_α radiation. Samples were contained in thin-walled Pyrex tubes sealed with picein wax, except for the lead compound which attacks glass readily. This substance was mixed with gum tragacanth and moistened with 40% aqueous hydrofluoric acid, and the resulting paste was smeared on a very fine glass rod.

The photographs of K_3HSnF_8 and K_3HPbF_8 were indexed by analogy with the known lattice parameters of K_3HNbOF_7. All the lines could be accounted for in this way, and in each case a consistent set of lattice parameters was calculated. The photograph of Na_3HTiF_8 was indexed with the help of the morphological axial ratios.

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[12] Ketelaar, *J. Chim. phys.*, 1948, **45**, 72.

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755. *Bisquaternary Ammonium Salts. Part IV.*[1] *3-Alkylbenzene-1,ω-bistrimethylammonium Salts.*

By J. N. ASHLEY and S. S. BERG.

A series of 3-alkylbenzene-1,ω-bistrimethylammonium di-iodides (I) has been prepared. These compounds are much less active as ganglion-blocking agents than are the corresponding isomers in the 4-alkylbenzene series.

SOME 4-alkylbenzene-1,ω-bistrialkylammonium di-iodides were described by Ashley and Leeds [1] in Part III of this series. Certain of these compounds were of interest as ganglion- or neuromuscular blocking agents, and in view of this it was decided to prepare some of the *m*-isomers, and of these the products where $n = 1$, 2, 3, and 4 were prepared and tested. The pharmacological results have been reported by Wien and Mason.[2] No compound of this *m*-series was as active as its *p*-isomer; when $n = 2$, the *m*-compound had only 50% of the ganglion-blocking activity of the corresponding *p*-isomer.[1,2]

(I) $m\text{-}Me_3N^+\cdot C_6H_4\cdot[CH_2]_n\cdot NMe_3^+ \ 2I^-$

The four compounds were prepared without difficulty; for the case where $n = 1$, 3-aminobenzyldimethylamine (prepared in excellent yield by modification of the methods used by Bennett and Willis [3] and Stedman [4]) was readily converted into the di-iodide (I;

[1] Part III, Ashley and Leeds, *J.*, 1957, 2706.
[2] Wien and Mason, *Brit. J. Pharmacol.*, 1953, **8**, 306.
[3] Bennett and Willis, *J.*, 1929, 264.
[4] Stedman, *J.*, 1927, 1906.

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$n = 1$) by methylation and quaternisation with methyl iodide and sodium carbonate in methanol.

In the other cases (I; $n = 2$, 3, and 4), the synthesis followed the lines used earlier by Ashley and Leeds:

$$m\text{-}NMe_2\cdot C_6H_4\cdot CO\cdot[CH_2]_{n-1}\cdot H \xrightarrow[S]{NHMe_2} m\text{-}NMe_2\cdot C_6H_4\cdot[CH_2]_{n-1}\cdot CS\cdot NMe_2$$
(II) (III)

$$\xrightarrow{LiAlH_4} m\text{-}NMe_2\cdot C_6H_4\cdot[CH_2]_n\cdot NMe_2 \quad (IV)$$

The ketones (II; $n = 2$—4) were prepared from the appropriate alkyl phenyl ketone by successive nitration, reduction, methylation, quaternisation, and distillation of the quaternary salt *in vacuo*.

The Kindler–Willgerodt reaction was used to convert the ketones (II; $n = 2$—4) into the thioamides (III) which were smoothly reduced to the diamines (IV) by lithium aluminium hydride. The bisquaternary salts (I; $n = 2$—4) were prepared by treating the diamines with methyl iodide. They were white, crystalline, water-soluble compounds. The use of charcoal at any stage during the purification of these salts gave pale yellow products. The synthesis of the corresponding pentane (IV; $n = 5$) was not completed and only 3-nitro-[5] and 3-amino-valerophenone[5] were prepared in this synthesis.

A few preliminary experiments were also carried out on a possible alternative route to the di-iodide (I; $n = 5$), but this was not pursued further than 4-dimethylaminobutyl chloride hydrochloride.

Experimental

NN-*Dimethyl*-3-*nitrobenzylamine*, b. p. 131—132°/11 mm., was prepared (96%) as described by Bennett and Willis.[3] The picrate (from ethanol) had m. p. 215—217°.

3-*Amino*-NN-*dimethylbenzylamine*.—The foregoing nitro-compound (8 g.) in methanol (40 ml.) was reduced catalytically by using Adams catalyst (0·4 g.). Reduction was complete in 2 hr. and gave the diamine (6·3 g., 96%), pale yellow needles, m. p. 44—46° [from light petroleum (b. p. 60—80°)] (Stedman,[4] who reduced the nitro-compound with tin and hydrochloric acid, gives m. p. 46°).

3-*Dimethylamino*-NN-*dimethylbenzylamine Bismethiodide*.—The above diamine (5·0 g.), methyl iodide (30 ml.), anhydrous sodium carbonate (3·6 g.), and methanol (30 ml.) were refluxed together for 6 hr. The solution, after being mixed with methanol (30 ml.), was cooled to 5°; the *product* was filtered off and recrystallised twice from ethanol, forming prisms (8 g., 52%), m. p. 194—195° (decomp.) (Found: N, 6·5; I, 54·6. $C_{13}H_{24}N_2I_2$ requires N, 6·7; I, 54·9%).

3-Nitrovalerophenone (66%), b. p. 135—136°/0·3 mm. (lit.,[5] 145—150°/3 mm.), d_{25} 1·155, 3-nitropropiophenone (58%), m. p. 96—98° (lit.,[6] 98°), 3-nitrobutyrophenone (36%), m. p. 61° (lit.,[7] 61—62°), 3-aminoacetophenone (90%), m. p. 95—97° (lit.,[8] 90·5°), 3-aminopropiophenone (89%), m. p. 41—43° (lit.,[7] 42°), b. p. 125—127°/9·5 mm., 3-aminobutyrophenone (77%), m. p. 26—28° (lit.,[7] 27—28°), b. p. 168—169°/9 mm., 3-aminovalerophenone (88%), b. p. 180—183° (bath-temp.)/10 mm. (lit.,[5] 160—163°/3 mm.), and 3-dimethylaminoacetophenone (71%), m. p. 40—43°, b. p. 145—147°/11 mm. (lit.,[9] m. p. 42—43°, b. p. 148°/13 mm.), were prepared by the recorded methods.

3-*Dimethylaminopropiophenone*.—3-Aminopropiophenone (35 g.), methyl iodide (105 ml.), anhydrous sodium carbonate (26 g.), and methanol (105 ml.) were refluxed overnight. The mixture was evaporated under reduced pressure and the residue was distilled at 15 mm. The distillate afforded 3-*dimethylaminopropiophenone* (35 g., 84%), m. p. 31—33°, b. p. 150°/10 mm. (Found: C, 74·2; H, 8·4; N, 7·6. $C_{11}H_{15}ON$ requires C, 74·6; H, 8·4; N, 7·9%). 3-*Dimethylaminobutyrophenone* (30 g., 85%), b. p. 163—164°/12 mm. (Found: C, 75·1; H, 8·9; N, 7·2. $C_{12}H_{17}ON$ requires C, 75·4; H, 8·9; N, 7·3%), was prepared similarly.

[5] Hartung and Munch, *J. Amer. Chem. Soc.*, 1929, **51**, 2570.
[6] Comanducci and Pescitelli, *Gazzetta*, 1906, **36**, 787.
[7] Elson, Gibson, and Johnson, *J.*, 1930, 1128.
[8] Camps, *Arch. Pharm.*, 1902, **240**, 1.
[9] Braun, Rupe, and Zembruski, *Ber.*, 1901, **34**, 3524.

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3-*Dimethylamino*-NN-*dimethylphenylthioacetamide*.—3-Dimethylaminoacetophenone (8·2 g.), redistilled dimethylamine (4·8 ml.), and sulphur (2·4 g.) were heated in a sealed tube at 160—165° for 4 hr. The resulting dark oil was extracted with benzene (5 × 50 ml.); the red solution, after being separated from tar, afforded an oil. Distillation of this at 0·2 mm. afforded two fractions: (*a*) (3·4 g.), b. p. 90—150° (bath-temp.) and (*b*) (5·2 g.), b. p. 150—160° (bath-temp.). Redistillation of the latter gave an oil (4·2 g.), b. p. 142—146°/0·1 mm., which slowly solidified and recrystallised from ether, giving the *thio-compound* (3·4 g., 26%), pale yellow needles, m. p. 63—64° (Found: C, 64·95; H, 8·05; N, 12·3. $C_{12}H_{18}N_2S$ requires C, 64·9; H, 8·1; N, 12·6%).

3-*Dimethylamino*-NN-*dimethylphenyl-thiopropionamide* (14·8%), b. p. 175—180° (bath-temp.)/0·2 mm. (Found: C, 65·7; H, 8·4; N, 12·1. $C_{13}H_{20}N_2S$ requires C, 66·1; H, 8·5; N, 11·9%) and *-thiobutyramide* (9·6%), b. p. 176—178°/0·1 mm. (Found: C, 67·5; H, 8·5; N, 11·0. $C_{14}H_{22}N_2S$ requires C, 67·2; H, 8·8; N, 11·2%), were prepared similarly, the sealed-tube reactions being carried out at 180°.

3-*Dimethylamino*-NN-*dimethylphenethylamine*.—3-Dimethylamino-*NN*-dimethylphenylthioacetamide (8·4 g.) in anhydrous ether (400 ml.) was added during 0·75 hr. to a stirred suspension of lithium aluminium hydride (2 g.) in anhydrous ether (100 ml.) at room temperature. The mixture was then stirred for 1 hr., water (30 ml.) was added, and the base extracted with 2N-hydrochloric acid. The diamine (6·4 g., 88·9%) was an oil, b. p. 85—90° (bath temp)/0·2 mm. (Found: C, 74·1, 74·4; H, 10·6, 10·5; N, 13·9. $C_{12}H_{20}N_2$ requires C, 75·0; H, 10·4; N, 14·0%). 3-*Dimethylamino*-NN-*dimethylphenyl-propylamine* (83%), b. p. 100—102°/0·8 mm. (Found: C, 75·3; H, 10·7; N, 11·3. $C_{13}H_{22}N_2$ requires C, 75·7; H, 10·7; N, 13·6%), and *-butylamine* (85%), b. p. 118—120°/0·7 mm. (Found: C, 76·6; H, 10·8; N, 12·9. $C_{14}H_{24}N_2$ requires C, 76·4; H, 10·9; N, 12·7%), were prepared similarly.

3-*Ethylbenzene*-1,2′-*bis*(*trimethylammonium Iodide*).—3-Dimethylamino-*NN*-dimethylphenethylamine (6·0 g.) and methyl iodide (20 ml.) were refluxed in methanol (100 ml.) for 5 hr., to give the bisquaternary *salt* which crystallised from methanol in rhombs (8 g., 54%), m. p. 231—233° (decomp.) (Found: N, 5·9; I, 53·0. $C_{14}H_{26}N_2I_2$ requires N, 5·9; I, 53·35%). 3-n-*Propylbenzene*-1,3′-*bis*(*trimethylammonium iodide*) [46·5% from methanol–acetone (1 : 3)], m. p. 197—198° (decomp.) (Found: N, 5·4; I, 51·6. $C_{15}H_{28}N_2I_2$ requires N, 5·7; I, 51·8%), and 3-n-*butylbenzene*-1,4′-*bis*(*trimethylammonium iodide*) [42%, from methanol–acetone (1 : 4)], m. p. 212—214° (decomp.) (Found: N, 5·5; I, 50·7. $C_{16}H_{30}N_2I_2$ requires N, 5·7; I, 50·4%), were prepared similarly.

4-*Dimethylaminobutyl Acetate*.—4-Bromobutyl acetate [10] (33·1 g., 24 ml.) and dimethylamine (16·8 g., 25 ml.) in toluene (50 ml.) were heated in a sealed tube at 100—110° for 4 hr. The contents were extracted with 10% hydrochloric acid; basification of the aqueous layer yielded 4-*dimethylaminobutyl acetate* (14·2 g., 54%), b. p. 89—90°/12 mm. (Found: C, 60·2; H, 10·8; N, 8·8. $C_8H_{17}O_2N$ requires C, 60·4; H, 10·7; N, 8·8%). The *picrate* formed yellow plates (from acetic acid), m. p. 199—200° (Found: N, 14·6. $C_8H_{17}O_2N,C_6H_3O_7N_3$ requires N, 14·4%).

4-*Dimethylaminobutanol*.—The above acetate (25 g.) was refluxed with potassium hydroxide (25 g.) in water (50 ml.) and ethanol (170 ml.) for 8 hr. and afforded the alcohol (17·8 g., 97%), b. p. 90°/12 mm. (Lukeš and Přeučil,[11] who prepared it by distilling 1,1-dimethylpyrrolidinium hydroxide, give b. p. 187—189°) (Found: C, 61·2; H, 12·8; N, 12·2. Calc. for $C_6H_{15}ON$: C, 61·5; N, 12·8; N, 12·0%). The *picrate* crystallised in yellow prisms (from ethanol), m. p. 77—78° (Found: N, 16·4. $C_6H_{15}ON,C_6H_3O_7N_3$ requires N, 16·6%).

4-*Dimethylaminobutyl Chloride Hydrochloride*.—Thionyl chloride (12·5 ml.) in anhydrous chloroform (50 ml.) was added during 0·5 hr. to the above alcohol (9·8 g.) in chloroform (17 ml.) at −10° to −5°. The solution was stirred for 2 hr. and the temperature allowed to rise to 25°. Removal of the solvent *in vacuo* at 20—25° left pale yellow, hydroscopic crystals (10·5 g., 74%). The *picrate* crystallised in yellow rhombs (from ethanol), m. p. 97—98° (Found: N, 15·4; Cl, 9·6. $C_6H_{14}NCl,C_6H_3O_7N_3$ requires N, 15·35; Cl, 9·7%).

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[10] Gold'Farb and Smoranski, *J. Gen. Chem. U.S.S.R.*, 1940, **10**, 113.
[11] Lukeš and Přeučil, *Coll. Czech. Chem. Comm.*, 1938, **10**, 384.

XUM

756. *The Nature of the Metal Complexes of 1,3-Diphenyltriazen.*

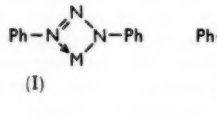
By C. M. Harris, B. F. Hoskins, and R. L. Martin.

The bivalent copper and palladium complexes of 1,3-diphenyltriazen (dpth) have been shown to exist as dimers (M_2 dpt_4) (M = Cu and Pd), in solvents such as benzene and nitrobenzene. The copper complex is diamagnetic, both in solution and in the solid state, and it is suggested that these compounds, as well as the analogous nickel complex, possess a bridged structure similar to that of copper(II) acetate. The diamagnetic nickel compound [Ni_2 dpt_4] forms paramagnetic (μ ~3·2 B.M.) adducts Ni dpt_2 py_2 and Ni dpt_2 phen with pyridine and 1,10-phenanthroline.

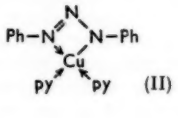
Quadricovalent palladium(II) complexes, Pd dpt_2 $dpth_2$, $PdCl_2$ $dpth_2$, and Pd dpt_2 phen, in which 1,3-diphenyltriazen and its derived anion function as unidentate groups, have also been prepared and examined.

It has long been known that various metals can displace the imino-hydrogen atom from 1,3-diphenyltriazen (diazoaminobenzene), and it has been suggested that both the parent "acid" (dpth) and the derived anion (dpt) function as bidentate chelating groups.[1,2] Dwyer [1] concluded that in the lemon-yellow silver(I) complex [3] Ag(dpt) the silver atom is co-ordinately saturated and that both this compound and the analogous copper(I) derivative [4] have structure (I). The dipyridine adduct Cu dpt py_2 was formulated as in (II).[1]

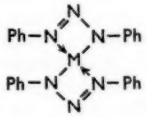
Bivalent metal complexes of the empirical formula M dpt_2 (where M = Cu,[1,4,5] Ni,[2] Pd,[1] and Hg [5-8]) have also been isolated. The copper and palladium complexes were assigned the uninuclear square-co-ordinated structure (III) on the basis of ebullioscopic molecular-weight measurements,[1] whereas the diamagnetic nickel compound was assigned structure (IV) because of its dimerism in freezing benzene.[2]



(I)

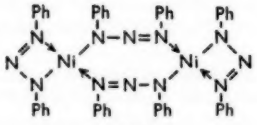


(II)

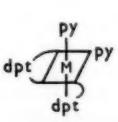


M = Cu(II) or Pd(II)

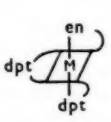
(III)



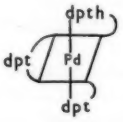
(IV)



(V)



(VI)



(VII)

In addition to the above bivalent metal complexes, the compounds M dpt_2 py_2 and M dpt_2 en (where M = Cu, Ni, or Pd, py = pyridine, and en = ethylenediamine) have also been described,[1,2] as well as an unstable palladium complex formulated as Pd dpt_2 dpth.[1] The palladium and nickel compounds have been assigned the sexicovalent structures (V—VII) in which the triazen molecule and its derived anion function as bidentate chelate

[1] Dwyer, *J. Amer. Chem. Soc.*, 1941, **63**, 78.
[2] Dwyer and Mellor, *ibid.*, p. 81.
[3] Griess, *Annalen*, 1862, **121**, 261; 1866, **137**, 53; see also ref. 8 and Meunier and Rigot, *Bull. Soc. chim. France*, 1900, **23**, 104.
[4] Meunier, *Compt. rend.*, 1900, **131**, 52; see also Niementowski and Roszkowski, *Z. phys. Chem.*, 1897, **22**, 145.
[5] Mangini and Dezudicibus, *Gazzetta*, 1933, **63**, 601.
[6] Cuisa and Pestalozza, *ibid.*, 1911, **41**, I, 394; *Atti R. Accad. Lincei*, 1911, **18**, II, 90.
[7] Veichiotte and Capondacqua, *Gazzetta*, 1925, **55**, 369.
[8] Watt and Fernelius, *Z. anorg. Chem.*, 1934, **221**, 187.

groups. Finally it may be noted that bivalent mercury forms both a bis-complex Hg dpt_2[2,5-8] as well as the dichloro-complex $HgCl_2$ $dpth_2$.[9-11]

The structures so far proposed for these metal–triazen complexes in general involve this ligand in a four-membered ring which might be expected, from a consideration of the valency angles, to be considerably strained. However, the palladium(II) and nickel(II) complexes are exceptionally stable and markedly indifferent to strongly co-ordinating ligands such as pyridine and ethylenediamine. Hence, it appears that the proposed structures are not completely compatible with the properties of these compounds and this fact coupled with their importance as accepted examples of four-membered chelate rings has led us to re-investigate their properties.

TABLE 1. *Metal complexes of* 1,3-*diphenyltriazen* (dpth).

Metal	Empirical formula	Colour	Molecular formula
Cu(I)	Cu dpt	Yellow or orange	Probably polymeric
Ag(I)	Ag dpt	Yellow	Probably polymeric
Cu(II)	Cu dpt_2	Dark-green	Cu_2 dpt_4
			Cu_2 dpt_4, CH_3OH *
Ni(II)	Ni dpt_2	Red	Ni_2 dpt_4
	Ni dpt_2 py_2	Yellow-brown	Probably polymeric
	Ni dpt_2 phen	,,	Probably polymeric *
Pd(II)	Pd dpt_2	Dark-brown	Pd_2 dpt_4
		,,	Pd_2 dpt_4, $0{\cdot}5C_6H_6$ *
		,,	Pd_2 dpt_4, $CH_3{\cdot}CO{\cdot}CH_3$ *
	$PdCl_2$ $dpth_2$	Orange-brown	$PdCl_2$ $dpth_2$, $0{\cdot}5CH_3{\cdot}CO{\cdot}CH_3$ *
	Pd dpt_2 $dpth_2$	Reddish-brown	Pd dpt_2 $dpth_2$,H_2O *
		,,	Pd dpt_2 $dpth_2$,$0{\cdot}5CH_3OH$ *
	Pd dpt_2 py_2	Orange	Pd dpt_2 py_2,C_5H_5N *
		,,	Pd dpt_2 py_2,C_6H_6 *
	Pd dpt_2 phen	Orange-brown	Pd dpt_2 phen *
		,,	Pd dpt_2 phen,$0{\cdot}5C_6H_6$ *
Hg(II)	Hg dpt_2	Yellow	Probably polymeric
	$HgCl_2$ $dpth_2$	,,	Probably polymeric

* These compounds are reported here for the first time.

TABLE 2. *Molecular weight of metal triazen complexes.*

Mol. formula	Method (all in C_6H_6)	Concn. (g./100 g.)	ΔT	Mol. wt. obs.	calc.
Cu_2 dpt_4	Cryosc.	0·39	0·021°	920	
		0·46	0·019	1180	
		0·39	0·020	960	910
	Ebull.[1]	1·35	0·038	930	
		0·91	0·023	1030	
Ni_2 dpt_4	Cryosc.	0·21	0·012	980	
	Ebull.	0·47	0·011	1100	900
Pd_2 dpt_4	Cryosc. $PhNO_2$	0·15	0·009	1160	
		0·12	0·007	1160	998
	Ebulliosc.	0·78	0·020	1020	
Pd dpt_2 $dpth_2$	Cryosc.[2]	0·22	0·031	780	
		0·43	0·055	825	893
Pd dpt_2 py_2	Cryosc.[3]	0·47	0·047	555	
		0·17	0·020	480	656

[1] In the ebullioscopic determinations, the green solution of the copper(II) complex decomposes with the formation of orange products after some minutes, and the b. p. slowly rises. B. p. elevations observed over the first 5 min., on the green solution, correspond to the dimeric formula.
[2] This compound was used as hydrate, in the presence of Na_2SO_4–Na_2SO_4,$10H_2O$.
[3] This compound was used as solvate containing 1 mol. of benzene.

The complexes of 1,3-diphenyltriazen with copper, nickel, palladium, silver, and mercury, which have been prepared and examined during this investigation, are listed in Table 1. The copper(II), nickel(II), and palladium(II) complexes of empirical formula M dpt_2 are listed as dimers on the basis of molecular-weight measurements (see Table 2).

[9] Hantzsch and Perkin, *Ber.*, 1897, **30**, 1412.
[10] Mandal, *Science and Culture*, 1940, **6**, 59.
[11] Knowles and Watt, *J. Amer. Chem. Soc.*, 1942, **64**, 935.

Many of the compounds displayed a marked tendency to crystallise with solvent of crystallisation which in some cases was not removed by heating them at reduced pressures. These compounds are all diamagnetic, with the exception of several of the nickel complexes whose magnetic moments are listed in Table 3.

The preparation and properties of the compounds in Table 1 are briefly outlined below, in order to contrast them with previous results, which in a number of cases are at variance with ours.

Copper(I) *and Silver*(I).—The copper and silver compounds of the type M dpt were prepared by Dwyer's method,[1] but were not sufficiently soluble in solvents other than pyridine for molecular-weight measurements. Although the copper(I) compound has been reported to be monomeric in boiling benzene,[1] we have been unable to repeat this measurement since the compound is not sufficiently soluble. Attempts to measure the molecular weight in camphor also failed owing to decomposition.

The silver compound has been reported to be monomeric in pyridine;[1] this, however, is a strong donor solvent which could be co-ordinated to the silver atom in solution. The compound is not sufficiently soluble in non-donor solvents for molecular-weight determinations.

Copper(II).—The dark green copper(II) complex was prepared as the solvate Cu_2 dpt_4, MeOH by treating copper(II) acetate with the ligand in methanol. The solvent-free complex was obtained by reprecipitating the compound from benzene with light petroleum. In the present work this compound has been shown to be dimeric from molecular-weight measurements in freezing benzene. The compound had been previously formulated[1] as the monomer on the basis of molecular complexities in bromoform as high as 1·5.

TABLE 3. *Magnetic susceptibility of metal–triazen complexes.*

Compound	Temp. (K)	$10^6\chi_g$	$10^6\Delta$ *	$10^6\chi_M$	μ (B.M.)
Cu_2 dpt_4	91°	0·14	−154	+281	0
	294	0·09	−154	+236	0
	359	0·12	−154	+263	0
Ni_2 dpt_4	294	−0·112	−156	+55	0
Ni dpt_2 py_2	300	6·91	−189	+4394	3·25
Ni dpt_2 phen	292	6·67	−207	+4417	3·23
Pd_2 dpt_4	294	—	—	Diamagn.‡	0
Pd dpt_2 $dpth_2$	294	−0·38	−157	−171	0
dpth	299	−0·167	—	−33	0
Cu_2 dpt_4 (benzene soln.†) (0·00685M)	294	−0·2	−154	Diamagn.	0

* Including diamagnetic correction for M^{++}. † Method as described by Martin and Whitley.[13]
‡ Insufficient for quantitative measurement.

Although this compound is diamagnetic, as is the above copper(I) complex, the absorption spectra of the copper(II) and copper(I) complexes are markedly different in the visible region. The copper(II) compound is characterised by a broad and unsymmetrical absorption maximum centred at ~625 mμ with ε 1850. Nitrogen-linked copper(II) complexes are well known to possess a broad absorption band in this region, although the extinction coefficients for these compounds are considerably lower.

Unlike the nickel(II) and palladium(II) derivatives discussed below, this compound is unstable in hot solvents, and presumably undergoes rapid self-reduction to orange-brown solutions of the copper(I) complex, as suggested by Dwyer.[1] Attempts to prepare the reported[1] indigo-blue dipyridine adduct Cu dpt_2 py_2 were unsuccessful, apparently owing to reduction of the compound.

Nickel(II).—The dipyridine compound, Ni dpt_2 py_2, was obtained by Dwyer's method,[2] and shown to be paramagnetic with a moment of $\mu = 3{\cdot}2$ B.M./Ni atom, corresponding to the presence of two unpaired electrons. It was found that this paramagnetic complex was readily converted, in refluxing toluene, into the red diamagnetic binuclear compound Ni_2 dpt_4. This compound had been prepared[2] by heating the solid dipyridine complex at 120—130° for 15 hours. A paramagnetic ($\mu = 3{\cdot}2$ B.M./Ni atom) 1,10-phenanthroline

complex, Ni dpt_2 phen, was obtained by refluxing the diamagnetic dimer with 1,10-phenanthroline in benzene. The molecular weight of the dimer was confirmed cryoscopically in benzene (see Table 2); the pyridine and phenanthroline derivatives were too insoluble for cryoscopic molecular-weight determinations.

Palladium(II).—On attempting to prepare the compound previously reported[1] as impure Pd dpt_2 dpth, we obtained the compound Pd dpt_2 $dpth_2$,H_2O. The water was readily replaced by half a molecule of methanol. This compound is monomeric in freezing benzene in the presence of sodium sulphate. When the compound is refluxed in acetone, it dissociates, forming the dimer, Pd_2 dpt_4,$COMe_2$. On precipitation from benzene with light petroleum, the acetone was replaced and the compound Pd_2 dpt_4,0·5C_6H_6 was obtained from which the benzene was removed at 180°. The solvent-free compound was shown to be binuclear by both cryoscopic and ebullioscopic molecular-weight measurements (see Table 2).

The orange crystalline compound, Pd dpt_2 py_2, py, was prepared by dissolving Pd dpt_2 $dpth_2$ in pyridine and precipitating the new compound by water. On dissolution of this compound in benzene and precipitation with light petroleum, the lattice pyridine was replaced by benzene. The benzene was not removed *in vacuo* at 100°. The compound is monomeric in benzene at the freezing point (see Table 2).

The 1,10-phenanthroline complex, Pd dpt_2 phen,0·5C_6H_6, was obtained by treating Pd dpt_2 $dpth_2$ with phenanthroline in warm benzene. The benzene was removed at 100° *in vacuo*. The dichloro-complex $PdCl_2$ $dpth_2$,0·5$COMe_2$ was also obtained by mixing potassium tetrachloropalladate(II) with diphenyltriazen in 50% aqueous acetone. This compound and the above phenanthroline complex were not sufficiently soluble for molecular-weight measurements.

Experimental

1,3-*Diphenyltriazen*.—Diazoaminobenzene (from British Drug Houses Ltd.) was purified by repeated recrystallisation from 50% ethanol containing a small amount of potassium hydroxide and carbon. It had m. p. 99—100° (Found: C, 72·9; H, 5·4; N, 21·2. Calc. for $C_{12}H_{11}N_3$: C, 73·1; H, 5·6; N, 21·3%).

Dichlorobis(1,3-*diphenyltriazen*)*palladium*(II).—A solution of 1,3-diphenyltriazen (0·5 g.) in 50% acetone (150 ml.) was added slowly with stirring to a 50% acetone solution (50 ml.) of potassium tetrachloropalladate (0·33 g.). The orange-brown *compound* which was deposited was filtered off, washed with 50% acetone, and dried at 100° (Found: C, 51·8; H, 4·0; N, 14·5; Cl, 11·9; Pd, 17·9. $C_{24}H_{22}N_6Cl_2Pd$,0·5C_3H_6O requires C, 51·0; H, 4·2; N, 14·0; Cl, 11·8; Pd, 17·7%). The acetone of crystallisation was not lost at 100°.

Bis-(1,3-*diphenyltriazenido*)*bis*-(1,3-*diphenyltriazen*)*palladium*(II).—This compound was prepared by dropwise addition of an ice-cold mixture of aqueous potassium tetrachloropalladate (3·3 g./35 ml.) and 3N-sodium acetate (15 ml.) to a chilled methanolic solution of the triazen (12 g./200 ml.). Almost immediately, reddish-brown crystals were deposited. The *compound* was filtered off, washed with ice-cold (80%) methanol, and dried *in vacuo* (P_2O_5) (Found: C, 62·9; H, 4·6; N, 18·1; Pd, 12·0. $C_{48}H_{42}N_{12}Pd$,H_2O requires C, 63·3; H, 4·9; N, 18·5; Pd, 11·7%). When this compound is dissolved in cold benzene and precipitated by a large excess of cold methanol the lattice water is replaced by 0·5 mole of methanol (Found: C, 64·0; H, 4·7; N, 18·0; Pd, 11·8. $C_{48}H_{42}N_{12}Pd$,0·5CH_3OH requires C, 64·0; H, 4·9; N, 18·5; Pd, 11·7%). This *methanolate* was extremely soluble in acetone, benzene, and nitrobenzene, and in acetone or benzene, particularly when heated, readily rearranged and gave a precipitate of μμ′μ″μ‴-tetrakis-(1,3-diphenyltriazenido)dipalladium(II).

μμ′μ″μ‴-*Tetrakis*-(1,3-*diphenyltriazenido*)*dipalladium*(II).—The compound bis-(1,3-diphenyltriazenido)bis-(1,3-diphenyltriazen)palladium(II) was refluxed in acetone for some time. The reddish-brown solution became dark brown, and a dark brown crystalline *product* was deposited (Found: Pd, 20·2, 20·4. $C_{48}H_{40}N_{12}Pd_2$,C_3H_6O requires Pd, 20·2%). Dissolution of this acetone solvate in benzene and precipitation by addition of light petroleum gave a dark brown *compound* (Found: C, 58·4; H, 3·9; N, 16·5; Pd, 20·4. $C_{48}H_{40}N_{12}Pd_2$,0·5C_6H_6 requires C, 59·1; H, 4·2; N, 16·2; Pd, 20·5%). The benzene was lost at 180° in 6 hr., giving the unsolvated *compound* (Found: C, 57·5; H, 3·8; N, 16·4; Pd, 21·5. $C_{48}H_{40}N_{12}Pd_2$ requires C,

57·8; H, 4·0; N, 16·9; Pd, 21·4%). This compound was sparingly soluble in most organic solvents, but insoluble in methanol and ethanol.

Bis-(1,3-diphenyltriazenido)dipyridinepalladium(II).—This was obtained as orange crystals containing a molecule of pyridine of crystallisation by the following method. Bis-(1,3-diphenyltriazenido)bis-(1,3-diphenyltriazen)palladium(II) was dissolved in cold pyridine, and the product precipitated by the addition of water. The orange crystals were reprecipitated three times from pyridine with water. The *compound* was dried over phosphoric oxide (Found: C, 63·8; H, 4·7; N, 16·7; Pd, 14·0. $C_{34}H_{30}N_8Pd,C_5H_5N$ requires C, 63·7; H, 4·8; N, 17·1; Pd, 14·4%). The lattice pyridine was replaced by benzene on dissolving this compound in benzene and precipitating the new solvate by light petroleum (Found: C, 64·8; H, 4·7; N, 15·2; Pd, 14·1. $C_{34}H_{30}N_8Pd,C_6H_6$ requires C, 65·3; H, 4·9; N, 15·3; Pd, 14·4%). The benzene was not lost at 100° *in vacuo* in 1 hr.

Bis-(1,3-diphenyltriazenido)-1,10-phenanthrolinepalladium(II).—Orange-brown crystals were obtained by treating Pd dpth$_2$ dpt$_2$ (0·47 g.) with 1,10-phenanthroline monohydrate (0·09 g.) in warm benzene. The *product* was filtered off and crystallised from benzene by addition of light petroleum (Found: C, 64·6; H, 4·2; N, 15·1; Pd, 14·9. $C_{36}H_{28}N_8Pd,0{\cdot}5C_6H_6$ requires C, 65·2; H, 4·4; N, 15·6; Pd, 14·8%). The benzene was removed at 100° *in vacuo* (Found: C, 63·9; H, 4·0; N, 15·9; Pd, 15·7. $C_{24}H_{28}N_8Pd$ requires C, 63·8; H, 4·2; N, 16·5; Pd, 15·7%). The solvent-free *compound* was slightly soluble in benzene and sparingly soluble in nitrobenzene.

Bis-(1,3-diphenyltriazenido)dipyridinenickel(II).—This compound was prepared by Dwyer and Mellor's method [2] (Found: C, 67·1; H, 4·8; N, 18·2; Ni, 9·5. Calc. for $C_{34}H_{30}N_8Ni$: C, 67·0; H, 4·9; N, 18·4; Ni, 9·6%).

μμ′μ″μ‴-*Tetrakis-(1,3-diphenyltriazenido)dinickel*(II).—This compound can be prepared by the method of Dwyer and Mellor,[2] heating the solid dipyridine complex at 120—130° for 10—15 hr. It is readily prepared by refluxing the dipyridine complex in toluene for 3 hr. The red solution was cooled, treated with an equal amount of light petroleum, and kept at 0° for some time. The red crystals were recrystallised twice from benzene solution by addition of alcohol and dried *in vacuo* (Found: C, 64·4; H, 4·4; N, 18·1; Ni, 12·9. Calc. for $C_{48}H_{40}N_{12}Ni_2$: C, 63·9; H, 4·5; N, 18·6; Ni, 13·0%). This compound was moderately soluble in benzene, toluene, and nitrobenzene, but insoluble in acetone, methanol, and ethanol.

Bis-(1,3-diphenyltriazenido)-1,10-phenanthrolinenickel(II).—A benzene solution of Ni_2 dpt$_4$ (0·5 g. in 15 ml.) was refluxed with excess of 1,10-phenanthroline monohydrate (*ca.* 0·5 g.) for ~4 hr., the colour changing from deep-red to dark brown, and brown crystals separating. The *product* recrystallised from a large volume of benzene (Found: N, 17·4; Ni, 9·3. $C_{36}H_{28}N_8Ni$ requires N, 17·7; Ni, 9·3%); it was only slightly soluble in benzene and nitrobenzene, and completely insoluble in methanol or ethanol.

μμ′μ″μ‴-*Tetrakis-(1,3-diphenyltriazenido)copper*(II).—This was prepared by treating copper(II) acetate monohydrate with a methanolic solution of the ligand, by Dwyer's method.[1] The dark green crystalline compound was washed with ice-cold methanol and dried *in vacuo* over phosphoric oxide. The analytical figures on four separate preparations indicated the presence of one molecule of either methanol or water (in the lattice) which was not removed at 100°/1 mm. (Found: C, 62·2; H, 4·3; N, 18·1; Cu, 13·8. $C_{48}H_{40}N_{12}Cu_2,CH_3{\cdot}OH$ requires C, 62·3; H, 4·7; N, 17·8; Cu, 13·5. $C_{48}H_{40}N_{12}Cu_2,H_2O$ requires C, 61·9; H, 4·6; N, 18·1; Cu, 13·7%). The solvent-free *dimer* was obtained by dissolving the above solvate in cold benzene and precipitating it by light petroleum (Found: C, 63·2; H, 4·5; N, 18·3. Calc. for $C_{48}H_{40}N_{12}Cu_2$: C, 63·2; H, 4·4; N, 18·4%). This was soluble in benzene and nitrobenzene, practically insoluble in methanol and ethanol, and very soluble in pyridine in which it rapidly decomposes.

1,3-*Diphenyltriazenidocopper*(I).—This was prepared by Dwyer's method,[1] with copper(I) iodide in place of copper(I) chloride. The lemon-yellow dipyridine complex was recrystallised twice from pyridine. The pyridine was then removed at 100° in 6 hr. (Found: C, 54·9; H, 3·9; N, 16·4; Cu, 24·3. Calc. for $C_{12}H_{10}N_3Cu$: C, 55·5; H, 3·9; N, 16·2; Cu, 24·5%). The compound was very sparingly soluble in benzene, toluene, acetone, nitrobenzene, and methyl and ethyl alcohol, but extremely soluble in pyridine.

1,3-*Diphenyltriazenidosilver*(I).—This compound was prepared by Dwyer's method [1] and recrystallised from pyridine–methanol (Found: C, 47·6; H, 3·2; N, 13·9; Ag, 35·4. Calc. for $C_{12}H_{10}N_3Ag$: C, 47·4; H, 3·3; N, 13·8; Ag, 35·5%). It was very sparingly soluble in benzene, nitrobenzene, nitromethane, and methyl cyanide although it dissolved readily in hot pyridine.

XUM

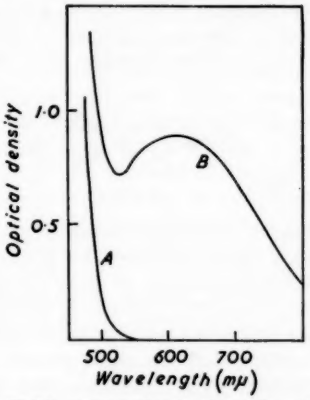
Bis-(1,3-diphenyltriazenido)mercury(II).—The bis-complex was prepared by treating mercuric acetate with the ligand in ethanol solution. It was purified by dissolution in pyridine–benzene (1 : 20) and precipitation by ethanol. The canary-yellow product was dried at 100° (Found: C, 48·5; H, 3·6; N, 14·3; Hg, 33·8. Calc. for $C_{24}H_{20}N_6Hg$: C, 48·6; H, 3·4; N, 14·2; Hg, 33·8%).

Dichlorobis-(1,3-diphenyltriazene)mercury(II).—An ethanolic solution of the ligand was added to a solution of mercury(II) chloride (0·69 g.) in alcohol. The orange precipitate was recrystallised from benzene by addition of light petroleum, and the orange-brown compound dried *in vacuo* (Found: C, 43·4; H, 3·1; N, 12·7. Calc. for $C_{24}H_{22}N_6Cl_2Hg$: C, 43·3; H, 3·3; N, 12·6%).

Molecular-weight Determinations.—Cryoscopic measurements were made by the conventional Beckmann method in the presence of 1—2 g. of sodium sulphate, containing a small amount of the decahydrate (see Robertson and Bury [12]) in order to keep a constant vapour pressure of water in both the benzene and the nitrobenzene solution. In a number of cases the determinations were also made in an enclosed moisture-free atmosphere in the all-glass cryoscope described elsewhere.[13] The experimental values quoted in Table 2 are sufficiently accurate to leave no doubt as to whether a compound is mono- or di-meric. However, when the observed depressions are small, the molecular weight values are probably not more accurate than *ca.* ±20%.

The ebulliometer used for molecular-weight determinations in boiling benzene was adapted from the design of Sucharda and Bobranski.[14]

Magnetic Measurements.—These were made on powdered samples, by the Gouy method in conjunction with a cryostat cooled by liquid nitrogen. The gram susceptibility χ_g, the molar susceptibility χ_M (corrected for the underlying diamagnetism of all atoms, Δ), and the magnetic moment μ, are set out in Table 3. The magnetic moment is calculated on the basis of a simple Curie law, $\mu = 2{\cdot}839[\chi_M T]^{0.5}$.



Visible spectra for Cu dpt (*A*) *and* Cu_2 dpt_4 (*B*) *in benzene solution* (M/2000) (1 *cm. cell*).

Electrical Conductivity.—The electrical conductivity of the above metal triazens, in nitro-benzene solution, was measured at room temperature by means of a Philips A. C. Wheatstone bridge (type G.M. 4249). The measurements were made at a 1000 c./sec., a Philips immersion cell (type G.M. 4221) with platinised electrodes being used. All the compounds were found to be non-electrolytes possessing molecular conductivities less than 0·1 mho at concentrations of $\sim 10^{-3}$molar.

Absorption Spectra in the Visible Region.—The absorption spectra of both copper complexes Cu dpt and Cu_2 dpt_4 and that of 1,3-diphenyltriazen in benzene solution were recorded between 4000 and 8000 Å, a Cary recording spectrophotometer (Model 11MS-50) being used. The two spectra are illustrated (the ligand did not absorb in this range).

Discussion

In view of the dimeric nature of the copper, nickel, and palladium complexes M_2 dpt_4, and the diamagnetism of the copper(II) complex, it is important to consider the possible bonding modes of the diphenyltriazenide anion and their structural implications.

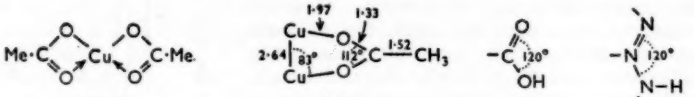
Recent work with copper(II) acetate is relevant. Lowry and French [15] first postulated that the acetate group functioned as a bidentate chelate, giving the 4-membered ring structure (VIII), but Sidgwick [16] criticized this on the grounds of considerable steric strain and distortion of natural valency angles. Even so, this structure continued to find favour until it was invalidated by the *X*-ray structure demonstration (Niekerk and

[12] Robertson and Bury, *J.*, 1923, **123**, 2037.
[13] Martin and Whitley, *J.*, 1958, 1394.
[14] Sucharda and Bobranski, *Chem. Ztg.*, 1927, **51**, 568.
[15] Lowry and French, *Proc. Roy. Soc.*, 1924, *A*, **106**, 489.
[16] Sidgwick, " The Electronic Theory of Valency," Oxford University Press, 1927, p. 253.

Schoening [17]) that the monohydrate was binuclear $[Cu(CH_3{\cdot}CO_2)_4(H_2O)_2]$, the pairs of contiguous copper atoms (Cu–Cu = 2·64 Å) being supported by four bridging acetate groups whose planes are at right angles. The molecular geometry is based on the 5-membered ring (IX), so that steric strain is eliminated.

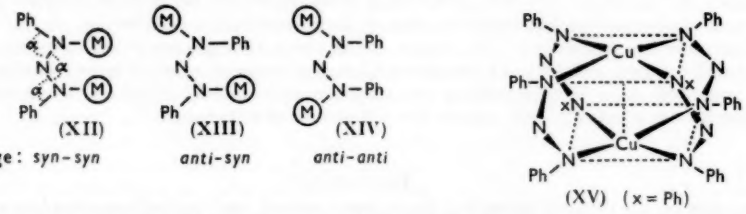
Although the structure of 1,3-diphenyltriazene is unknown, it will be apparent from diagrams (X) and (XI) that the geometry of the carboxy-group in fatty acids, which is based on sp^2-hybridisation of the C atom, is likely to parallel closely that of the N_3H group in diphenyltriazen. Further, the three potential bonding modes (XII—XIV) [based on (XI)] are possible if we assume that each diphenyltriazenide anion is bound to two metal atoms.

A molecular structure based on the *syn–syn*-bonding arrangement (XII) would lead to close approach of the two copper atoms, and the magnetic moment of the copper atoms could well be modified. In fact, the compound bis-(1,3-diphenylditriazenido)copper(II) has recently [18] been shown to be diamagnetic both in the solid state (between 80° and 400° K) and in benzene solution (at 20° C). Although, the observed diamagnetism in the solid state could conceivably arise from intermolecular Cu–Cu interactions, it is clear that, in



(VIII) (IX) (X) (XI)

benzene solution, intramolecular exchange interaction between copper atoms must occur to a degree sufficient for complete pairing of the unpaired electron associated with the $3d^9$-configuration of each bivalent copper atom. The exchange demagnetisation must arise from the presence of a direct Cu–Cu covalent bond in the dimeric molecule, Cu_2 dpt_4 for which we propose the structure (XV) based on *syn–syn*-bonding. Molecular models confirm that the eight phenyl groups, when suitably orientated, can be accommodated without steric hindrance, but that the terminal positions at each copper atom are not accessible for donor ligands. The observed diamagnetism is unique for copper(II) compounds at room temperature. We now believe the dimeric and diamagnetic nickel and palladium compounds Ni_2 dpt_4 and Pd_2 dpt_4 possess similar binuclear bridged structures, but that their diamagnetism is not diagnostic for the presence of metal–metal interaction



(XII) (XIII) (XIV) (XV) (x = Ph)

Bridge: *syn–syn* *anti–syn* *anti–anti*

since square-co-ordinated nickel(II) and palladium(II) complexes are invariably diamagnetic.

In contrast to the bridged Cu(II) complex, which tends to decompose in hot solvents, the nickel(II) and palladium(II) complexes are thermally rather stable, in the solid state and in solution. Further, the nickel and palladium complexes are comparatively inert to donor solvents such as pyridine, from which they recrystallise unchanged. The nickel complex Ni_2 dpt_4 can be converted into the dipyridine derivative Ni dpt_2 py_2 by prolonged boiling in pyridine. This is compatible with a binuclear structure similar to (XV) in that access to the metal atom is sterically hindered by phenyl groups.

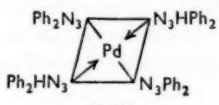
[17] Niekerk and Schoening, *Acta, Cryst.*, 1953, **6**, 227.
[18] Harris and Martin, *Proc. Chem. Soc.*, 1958, 259.

XUM

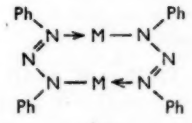
It is worth noting in connexion with the preparation of these complexes that the method of preparation of the copper(II) compound involves direct replacement of acetate bridges in binuclear $Cu_2(CH_3{\cdot}CO_2)_4$ by the triazen in methanol solution. Further, the binuclear nickel(II) complex cannot be obtained in this manner since binuclear nickel(II) acetate is unknown.

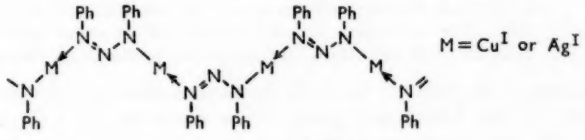
It remains to discuss the possible structures of the remaining metal–triazen complexes whose structures cannot be as readily inferred as those of the above bridged compounds. The triazen ligand need not necessarily function as a bridge between two metal atoms as in (XII—XIV) but can conceivably function as a neutral or negatively charged unidentate group.

In the case of palladium(II), the unstable and impure compound Pd dpt_2 dpth was postulated to have probably an octahedrally co-ordinated palladium(II) atom, the triazen functioning as a chelate group. Further, the compound was claimed [1] as the first example of sexicovalent palladium(II). Repeated attempts by the present authors to prepare this compound always yielded Pd dpt_2 $dpth_2$ containing either 1 mol. of water or 0·5 mol. of methanol trapped in the lattice. This compound is monomeric in freezing benzene. Bivalent palladium is nearly always square-co-ordinated in its compounds and although some recent evidence of its possessing a distorted octahedral structure has been reported,[19] the latter configuration is not common. The compound Pd dpt_2 $dpth_2$ can be adequately formulated as containing square-co-ordinated palladium on the basis that both the ligand (dpth) and its anion (dpt) function as unidentate groups through one of the triazen nitrogen atoms (see XVI). Also the compounds Pd phen dpt_2, Pd py_2 dpt_2, and $PdCl_2$ $dpth_2$ can be similarly formulated as square-co-ordinated monomers. The dipyridine compound was monomeric in freezing benzene; the other compounds were not sufficiently soluble for molecular-weight measurements.



(XVI)


(XVII)



(XVIII)

In contrast to the corresponding diamagnetic palladium(II) compounds, the bivalent nickel compounds Ni dpt_2 py_2 and Ni dpt_2 phen are paramagnetic with magnetic moments ($\mu \sim 3{\cdot}2$ B.M./Ni) corresponding to two unpaired electrons. This excludes a square($3d4s4p^2$) arrangement and would suggest an octahedral $4s4p^34d^2$ one, although a tetrahedral configuration ($4s4p^3$) is also possible. Since these compounds are not sufficiently soluble for molecular-weight measurements it is probable that they possess polymeric octahedral structures based on the bridging arrangement (XIII) or (XIV)

The copper(I) and silver(I) compounds M dpt have been previously formulated [1] as bicovalent monomers involving the metal atom in bond angles of 90° (see I). However, all bicovalent copper(I) and silver(I) compounds examined structurally have been shown to be linear and, further, the four-membered ring arrangement indicated in (I) would lead to considerable steric strain. A dimeric structure as in (XVII) based on *syn–syn*-bonding XII) would permit linear co-ordination about the metal atoms.* Also, polymeric

* The postulated structure (XVII) has been recently verified for Cu dpt by Brown and Dunitz (Internat. Conference on Co-ordination Chemistry, London, April, 1959). The intramolecular Cu–Cu separation was reported as 2·6 Å.

[19] Harris and Nyholm, *J.*, 1956, 4375; Harris, Nyholm, and Stephenson, *Nature*, 1956, **177**, 1127; Harris, Livingstone, and Reece, *Austral. J. Chem.*, 1957, **10**, 282; Harris, Livingstone, and Reece, *J.*, 1959, 1505.

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structures based on (XIII) or (XIV) would enable the metal to be linearly co-ordinated. One such possible structure is (XVIII). It was not possible to differentiate between these structures by molecular-weight measurements since the copper(I) compound and the analogous silver compound were insufficiently soluble in boiling benzene.

Finally, it is interesting to contrast the slightly soluble mercury compound $Hg\ dpt_2$ with the dimeric Cu(II), Ni(II), and Pd(II) compounds. Mercury(II) in its quadricovalent complexes is tetrahedral, and such a bonding arrangement would not permit the mercury(II) compound to exist in the dimeric bridged form. However, a polymeric structure involving tetrahedral mercury is most likely. The dichloro-complex $HgCl_2$ 2dpth was also insufficiently soluble at the freezing point to permit molecular-weight measurements.

In conclusion, it appears that there is no substantial evidence that 1,3-diphenyltriazen can chelate to metals to give four-membered rings. In fact, the information adduced regarding the structures of the binuclear copper(II), nickel(II), and palladium(II) complexes strongly supports the *syn–syn*-bridging. The remaining bivalent palladium complexes can be adequately interpreted in terms of square rather than octahedral palladium(II) with the ligand or derived anion functioning as a unidentate group.

The authors are indebted to Dr. E. Challen for carrying out many microanalytical determinations for carbon, hydrogen, and nitrogen. One of them (B. F. H.) thanks the Australian Atomic Energy Commission for study leave.

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757. *Stereochemistry of Reduction Products of* 1-*Acetyl-lycorin-2-one.*

By Yuzo Nakagawa and Shojiro Uyeo.

The isolated double bond in lycorine (I; R = R′ = H) has been unequivocally fixed by interconversion of the alkaloid and 1-*O*-acetyl-lycorin-2-one (II). The absolute stereochemistry of lycorine and 2-epilycorine (IV; R = R′ = H) and their hydrogenation products has been elucidated.

Recently, we showed [1] that the isolated double bond in lycorine (I; R = R′ = H) is allylic to the 2-hydroxyl group, since oxidation of 1-*O*-acetyl-lycorine (I; R = Ac, R′ = H) with manganese dioxide gave 1-*O*-acetyl-lycorin-2-one (II) (identified by the ultraviolet and infrared spectra).

Takeda and Kotera [2] previously assigned a diaxial conformation to the hydroxyl groups in dihydrolycorine, in agreement with our experimental results described below. In view of this, one might have assumed that 1-*O*-acetyl-lycorin-2-one was a product of epimerisation at position 1 during the oxidation of 1-*O*-acetyl-lycorine, *i.e.*, that the axial acetoxyl group was inverted, as a result of keto–enol tautomerism, to an equatorial configuration which is generally supposed to be the more stable. This possibility was, however, ruled out, since hydrogenation of 1-*O*-acetyl-lycorin-2-one (II) with Adams catalyst in acetic acid afforded 1-*O*-acetyldihydrolycorine (III; R = Ac), convertible by hydrolysis to the known dihydrolycorine (III; R = H).

Another possibility which merited more serious consideration was that the double bond in lycorine was actually at position 3a,4 and shifted to the adjacent position (3,3a) only when 1-*O*-acetyl-lycorine was oxidised to the ketone (II). However, reduction of the ketone (II) with sodium borohydride followed by hydrolysis yielded lycorine along with its epimer, 2-epilycorine (IV; R = R′ = H). Since migration of a double bond during this sort of reaction is highly improbable, it is certain that the double bond in lycorine is at the same place as that in 1-*O*-acetyl-lycorin-2-one (II) and accordingly was not affected in

[1] Nakagawa, Uyeo, and Yajima, *Chem. and Ind.*, 1956, 1238.
[2] Takeda and Kotera, *ibid.*, p. 347; *Pharm. Bull.* (*Japan*), 1957, **5**, 234.

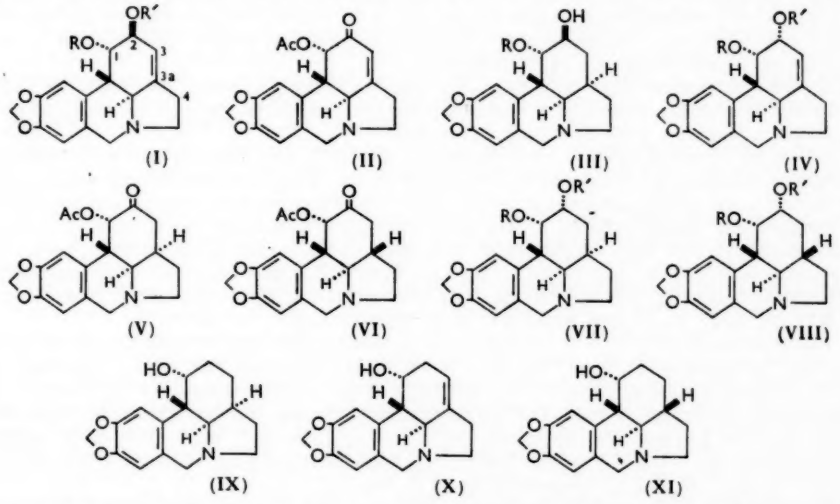
the course of transformation into the latter. Thus the position of double bond in lycorine has been fixed conclusively at position 3,3a rather than 3a,4.

2-Epilycorine (IV; R = R′ = H), which was also obtained from 1-*O*-acetyl-lycorin-2-one (II) by treatment with lithium aluminium hydride as the only isolable product, gave on condensation with acetone an isopropylidene derivative (IV; R, R′ = CMe_2<), while all attempts to obtain an analogous derivative from lycorine were unsuccessful. Therefore the two hydroxyl groups in 2-epilycorine are *cis* to each other. Since the hydroxyl group allylic to the double bond in 2-epilycorine was inferred from the route of formation to have a quasi-equatorial conformation, the adjacent *cis*-1-hydroxyl group must be axial. Consequently the hydroxyl groups are *trans* and diaxial in lycorine whose configuration differs from that of 2-epilycorine only in respect of the allylic hydroxyl group. This conclusion is in accord with the stereochemistry of dihydrolycorine advanced by Takeda and Kotera [2] who formulated it as (III; R = H) or its mirror image. If Mills's rule [3] concerning absolute configurations of allylic alcohols is valid for this series, the absolute configuration of lycorine can be represented by the formula (I; R = R′ = H), since, as shown in the annexed Table, lycorine and its acetate have molecular rotations more positive than those of their 2-epimers.

Optical rotations $[M]_D$ *of lycorine and its derivatives.*

Lycorine	−261°	2-Epilycorine	−623°
Diacetyl-lycorine	+117°	Diacetyl-2-epilycorine	−588°

Hydrogenation of 2-epilycorine in ethanol over palladium–carbon gave two products, α- and β-dihydro-2-epilycorine (VII and VIII respectively; R = R′ = H), the latter somewhat predominating. On the other hand, α-dihydro-2-epilycorine was the main product when the hydrogenation was carried out in acetic acid over Adams catalyst. These results parallel the case of caranine [4] (X) which lacks a 2-hydroxyl group 8 but is



(I) (II) (III) (IV) (V) (VI) (VII) (VIII) (IX) (X) (XI)

otherwise identical with lycorine. It was therefore considered probable that the stereochemistry of the ring systems of α- and β-dihydro-2-epilycorine was identical with that of α- and β-dihydrocaranine (IX and XI), respectively. This inference has been proved by converting the lycorine into the caranine compounds by treatment of the monotoluene-*p*-sulphonates (VII and VIII; R = H, R′ = *p*-$C_6H_4Me{\cdot}SO_2$) with lithium aluminium

[3] Mills, *J.*, 1952, 4976.
[4] Warnhoff and Wildman, *J. Amer. Chem. Soc.*, 1957, **79**, 2192.

hydride. It is concluded that the quasi-equatorial hydroxyl group allylic to the double bond in 2-epilycorine is less effective in directing the orientation of the entering hydrogen atoms to the double bond than the quasi-axial 2-hydroxyl group in lycorine which invariably gave on hydrogenation under varying conditions the known dihydrolycorine belonging to the α-dihydrocaranine series. Our attempt to obtain an epimer of dihydrolycorine having the ring system of β-dihydrocaranine and diaxial hydroxyl groups was unsuccessful. Hydrogenation of 1-*O*-acetyl-lycorine-2-one with palladium–carbon afforded predominantly 1-*O*-acetyl-β-dihydrolycorin-2-one (VI) which on reduction with lithium aluminium hydride or on hydrogenation in acetic acid over Adams catalyst followed by hydrolysis gave β-dihydro-2-epilycorine (VIII; R = R′ = H). The minor product of the hydrogenation of 1-*O*-acetyl-lycorin-2-one was 1-*O*-acetyl-α-dihydrolycorin-2-one (V), since it gave α-dihydro-2-epilycorine (VII; R = R′ = H) on treatment with lithium aluminium hydride.

Experimental

1-O-*Acetyl-lycorine* (I; R = Ac, R′ = H).—Di-*O*-acetyl-lycorine (I; R = R′ = Ac) (200 mg.) in methanol (25 ml.) and 35% hydrochloric acid (5 ml.) was heated on a water-bath for exactly 5 min. After cooling, the mixture was cautiously neutralised with aqueous sodium hydroxide, concentrated, diluted with aqueous ammonia, and extracted with ether. Lycorine (60 mg.) which remained undissolved was filtered off, and the ethereal extract dried and evaporated to give a residue which was chromatographed in benzene over alumina. The chloroform eluate gave 1-O-*acetyl-lycorine* (100 mg.), prisms (from ethanol), m. p. 215—216°, $[\alpha]_D$ −69·3° (*c* 0·95 in EtOH), $\nu_{max.}$ 3610 (OH) and 1733 cm.$^{-1}$ (OAc) in $CHCl_3$, $\lambda_{max.}$ 240 and 290 mμ (log ε 3·60 and 3·70) in EtOH (Found: C, 65·8; H, 5·7; N, 4·1; Ac, 12·9. $C_{18}H_{19}O_5N$ requires C, 65·6; H, 5·8; N, 4·3; Ac, 13·1%). The *hydrochloride* formed needles (from ethanol), m. p. 266° (decomp.) (Found: C, 55·2; H, 5·8; N, 3·4. $C_{18}H_{19}O_5N$,HCl,1·5H_2O requires C, 55·0; H, 5·9; N, 3·6%).

Lycorine from 1-O-*Acetyl-lycorine*.—1-*O*-Acetyl-lycorine (80 mg.) was saponified under reflux in 5% ethanolic potassium hydroxide (10 ml.) for 0·5 hr. After evaporation of the mixture, water was added, and the precipitate which formed was crystallised from ethanol to give lycorine, m. p. and mixed m. p. 277° (decomp.).

Di-O-*acetyl-lycorine from* 1-O-*Acetyl-lycorine*.—1-*O*-Acetyl-lycorine (50 mg.) in acetic anhydride (2 ml.) was heated on a water-bath for 1 hr. to furnish diacetyl-lycorine (50 mg.), m. p. and mixed m. p. 215—216° (from ethanol).

1-O-*Acetyl-lycorin-2-one* (II).—1-*O*-Acetyl-lycorine (300 mg.) was stirred with activated manganese dioxide (2 g.) in chloroform (30 ml.) for 16 hr. The manganese dioxide was removed by filtration, the filtrate was treated with charcoal and evaporated to dryness, and the residue in benzene was passed through a column of alumina. A benzene eluate gave 1-O-*acetyl-lycorin-2-one* (II) (100 mg.), which formed cubic crystals (from ethanol–chloroform), m. p. 191° (decomp.), $[\alpha]_D$ −323·8° (*c* 1·1 in $CHCl_3$), $\nu_{max.}$ 1739 (OAc) and 1675 cm.$^{-1}$ (αβ-unsaturated carbonyl) in Nujol, $\lambda_{max.}$ 235 and 290 mμ (log ε 4·20 and 3·70) in EtOH (Found: C, 65·8; H, 5·3; N, 4·5; Ac, 13·1. $C_{18}H_{17}O_5N$ requires C, 66·1; H, 5·2; N, 4·3; Ac, 13·2%).

Dihydrolycorine (III; R = H) *from* 1-O-*Acetyl-lycorin-2-one* (II).—1-*O*-Acetyl-lycorin-2-one (305 mg.) in acetic acid (20 ml.) was stirred with Adams catalyst (150 mg.) in hydrogen for 2·5 hr. (hydrogen uptake: 48 ml. Calc. for $2H_2$: 44 ml.). After removal of the catalyst, the mixture was evaporated *in vacuo* and the residue made alkaline and extracted with chloroform which afforded 1-O-*acetyldihydrolycorine* (III; R = Ac) (95 mg.), m. p. 199—200°, needles (from alcohol), $[\alpha]_D$ −126·1° (*c* 0·92 in $CHCl_3$), $\nu_{max.}$ 3030 (OH), 1730 cm.$^{-1}$ (OAc) in Nujol (Found: C, 65·4; H, 6·5. $C_{18}H_{21}O_5N$ requires C, 65·2; H, 6·4%).

Hydrolysis of 1-*O*-acetyldihydrolycorine (20 mg.) with 2% ethanolic sodium hydroxide (10 ml.) for 50 min. on the water-bath yielded dihydrolycorine (III; R = H), m. p. and mixed m. p. 255° (decomp.). The infrared spectrum was also identical with that of an authentic specimen.

Reduction of 1-O-*Acetyl-lycorin-2-one by Lithium Aluminium Hydride*.—1-*O*-Acetyl-lycorin-2-one (II) (100 mg.) and lithium aluminium hydride (50 mg.) in dry tetrahydrofuran (25 ml.) were kept at room temperature for 0·5 hr. and then heated on a water-bath for further 20 min. After cooling, the excess of the reagent was destroyed by dropwise addition of water and the

mixture was filtered. The filtrate was evaporated under reduced pressure, and the residue chromatographed in chloroform over alumina. Elution with chloroform furnished 2-epilycorine (IV; R = R′ = H) (75 mg.), m. p. 167—168°, needles (from isopropyl alcohol), $[\alpha]_D$ −217·0° (*c* 1·1 in $CHCl_3$), $\lambda_{max.}$ 290 mμ (log ε 3·67), $\nu_{max.}$ 3472 and 3413 cm.$^{-1}$ (OH) (Found: C, 66·7; H, 6·0; N, 5·1. $C_{16}H_{17}O_4N$ requires C, 66·9; H, 6·0; N, 4·9%).

Di-O-acetyl-2-epilycorine (IV; R = R′ = Ac).—2-Epilycorine (100 mg.) in pyridine (7 ml.) and acetic anhydride (200 mg.) was kept at room temperature for 42 hr. The mixture was added to water (20 ml.), basified with aqueous ammonia, and extracted with chloroform. The chloroform extract was washed with water, dried, and concentrated and the residue in benzene was passed through alumina to furnish *di-O-acetyl-2-epilycorine* (20 mg.), needles (from alcohol), m. p. 192—194·5°, $[\alpha]_D$ −158·2° (*c* 1·04 in $CHCl_3$), $\nu_{max.}$ 1733 cm.$^{-1}$ (OAc) in Nujol [Found: C, 65·0; H, 5·6; N, 3·9; Ac, 23·2. $C_{16}H_{15}O_4N(CH_3{\cdot}CO)_2$ requires C, 64·7; H, 5·7; N, 3·8; 2Ac, 23·2%].

Reduction of 1-*Acetyl-lycorin-2-one by Sodium Borohydride.*—1-*O*-Acetyl-lycorin-2-one (100 mg.) and sodium borohydride (50 mg.) in tetrahydrofuran (30 ml.) and water (2 ml.) were kept at room temperature for 48 hr. The excess of the reagent was destroyed by acetic acid, the mixture evaporated under reduced pressure, and the residue basified with aqueous ammonia and extracted with chloroform. The extract was washed with water, dried, and concentrated. Hydrolysis of the residue (80 mg.) on a water-bath in 10% ethanolic sodium hydroxide (20 ml.) for 15 min. afforded lycorine (20 mg.), m. p. 275° (from alcohol), identical with an authentic specimen in mixed m. p. and infrared spectrum. The mother-liquor gave a residue which, on crystallisation from isopropyl alcohol, afforded 2-epilycorine (40 mg.), m. p. 160—163°; acetylation of this with acetic anhydride (50 mg.) and pyridine (5 ml.) at room temperature for 5 days gave di-*O*-acetyl-2-epilycorine, m. p. and mixed m. p. 193—194° (superimposable infrared spectrum).

Isopropylidene-2-epilycorine (IV; R, R′ = CMe_2<).—Anhydrous zinc chloride (2 g.) and phosphoric acid (0·5 ml.) in dry acetone (5 ml.) were added dropwise to a stirred solution of 2-epilycorine (70 mg.) in dry acetone (10 ml.). After 45 hours' stirring at room temperature, potassium carbonate (2 g.) and water (2 g.) were added in one portion with cooling in ice, and stirring was continued for an additional hour. After removal of the solid, the acetone was evaporated and the residue extracted with chloroform. The chloroform extract was passed through alumina; the eluate furnished the *isopropylidene derivative* (IV; R, R′ = CMe_2<) (70 mg.), needles (from alcohol), m. p. 184—186°, $[\alpha]_D$ −191·5° (*c* 0·66 in $CHCl_3$), $\lambda_{max.}$ 235 and 290 mμ (log ε 3·51 and 3·61), $\nu_{max.}$ 1364 cm.$^{-1}$ (=CMe_2) in Nujol (Found: C, 70·2; H, 6·6; N, 4·2. $C_{19}H_{21}O_4N$ requires C, 69·7; H, 6·5; N, 4·3%).

Treatment of lycorine (100 mg.) with dry acetone (5 ml.), zinc chloride (2 g.), and phosphoric acid (0·5 ml.) for 48 hr. in a similar manner furnished the starting material in almost quantitative yield.

Hydrolysis of Isopropylidene-2-epilycorine.—Treatment of the isopropylidene derivative (IV; R, R′ = CMe_2<) (10 mg.) with 5% sulphuric acid (2 ml.) on a water-bath for 0·5 hr. regenerated 2-epilycorine (5 mg.), m. p. and mixed m. p. 167—168°.

Hydrogenation of 2-Epilycorine.—(*a*) 2-Epilycorine (300 mg.) in ethanol (20 ml.) was stirred in hydrogen in the presence of 10% palladium–carbon (300 mg.) for 2 hr. After removal of the catalyst, the solvent was evaporated under reduced pressure of nitrogen, and the residue was extracted with chloroform after addition of aqueous ammonia. The chloroform extract was dried and evaporated, and the residue (150 mg.) was chromatographed in benzene over alumina. The chloroform eluate (50 ml.) gave β-*dihydro-2-epilycorine* (VIII; R = R′ = H) (50 mg.) which formed needles (from ethyl methyl ketone), m. p. 146—147°, $[\alpha]_D$ −175·8° (*c* 0·8 in $CHCl_3$) (Found: C, 64·5; H, 6·5. $C_{16}H_{19}O_4N,\frac{1}{2}H_2O$ requires C, 64·4; H, 6·8%). The acetone eluate furnished α-*dihydro-2-epilycorine* (30 mg.), needles (from acetone), m. p. 196—197°, $[\alpha]_D$ −136·9° (*c* 0·9 in EtOH) (Found: C, 64·6; H, 6·5. $C_{16}H_{19}O_4N,\frac{1}{2}H_2O$ requires C, 64·4; H, 6·8%).

(*b*) 2-Epilycorine (250 mg.) in acetic acid (20 ml.) was hydrogenated with Adams catalyst (50 mg.) for 2 hr. After removal of the catalyst, the solvent was evaporated under reduced pressure under nitrogen, aqueous ammonia was added to the residue, and the mixture extracted with chloroform. A portion (50 mg.) of α-dihydro-2-epilycorine produced remained undissolved in the solvent and was collected by filtration. The chloroform extract was evaporated and the residue crystallised from acetone, to give a further crop of α-dihydro-2-epilycorine

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(150 mg.), m. p. and mixed m. p. 196—197°. The mother-liquor gave material whence crystallisation from ethyl methyl ketone afforded β-dihydro-2-epilycorine (15 mg.), m. p. and mixed m. p. 146—147°.

α-Dihydrocaranine from α-Dihydro-2-epilycorine.—α-Dihydro-2-epilycorine (80 mg.) and toluene-*p*-sulphonyl chloride (120 mg.) in pyridine (1 ml.) were kept at 17—21° for 18 hr. After evaporation of the pyridine under reduced pressure under nitrogen, aqueous ammonia was added to the residue and the whole was extracted with chloroform. The dried extract was evaporated and chromatographed in benzene over alumina. A benzene eluate furnished the *monotoluene*-p-*sulphonate* (VII; R = H, R′ = *p*-$C_6H_4Me{\cdot}SO_2$) (60 mg.), needles (from ethyl methyl ketone), m. p. 174° (Found: C, 60·5; H, 5·5. $C_{22}H_{25}O_6NS,\frac{2}{3}H_2O$ requires C, 60·6; H, 5·8%).

This toluene-*p*-sulphonate (100 mg.) in dry tetrahydrofuran (10 ml.) was added dropwise to lithium aluminium hydride (70 mg.) in dry tetrahydrofuran (10 ml.), and the mixture was refluxed for 10 hr. The excess of the reagent was destroyed by a little water, and the clear filtrate was evaporated to dryness under nitrogen under reduced pressure. The residue was taken up in 10% hydrochloric acid, washed with ether, made alkaline with aqueous ammonia, and extracted with chloroform. Evaporation of the chloroform, and chromatography of the residue (50 mg.) in chloroform over alumina furnished from a chloroform eluate α-dihydrocaranine (IX), needles (from acetone), m. p. 166—169° (20 mg.), identical with an authentic specimen in m. p., mixed m. p., and infrared spectrum.

β-Dihydrocaranine (XI).—β-Dihydro-2-epilycorine (VIII; R = R′ = H) (200 mg.) and toluene-*p*-sulphonyl chloride (200 mg.) in dry pyridine (4 ml.) were kept at 21° for 19 hr. After evaporation of pyridine under reduced pressure under nitrogen, the residue was made alkaline with aqueous ammonia and extracted with chloroform. The toluene-*p*-sulphonate (130 mg.) was not obtained crystalline even after chromatography.

The crude toluene-*p*-sulphonate (130 mg.) in dry tetrahydrofuran (15 ml.) was treated with lithium aluminium hydride (70 mg.) in dry tetrahydrofuran (10 ml.) under reflux for 9 hr. Working up as described above, followed by repeated chromatography over alumina with benzene–ether (2 : 1) as eluant, gave β-dihydrocaranine in a low yield (7 mg.). It crystallised from ethyl acetate as prisms, m. p. 164—165°, identical in mixed m. p. and infrared spectrum with an authentic specimen.

Hydrogenation of 1-O-*Acetyl-lycorin*-2-*one with Palladium–Carbon.*—The ketone (1 g.) in dioxan (50 ml.) was stirred in hydrogen in the presence of palladium–carbon (1 g.) for 5 hr. Hydrogen uptake was 85 ml. (calc. for $1H_2$: 72 ml.).

After removal of the catalyst, the solvent was evaporated to dryness under reduced pressure under nitrogen, and the residue chromatographed in benzene over alumina. The first benzene eluate furnished 1-O-*acetyl-α-dihydrolycorinone* (V) (30 mg.) which after crystallisation from propan-2-ol had m. p. 196—197°, $[\alpha]_D$ −262·0° (*c* 0·68 in $CHCl_3$), $\lambda_{max.}$ 236 and 292 mμ (log ε 3·50 and 3·60) in EtOH, $\nu_{max.}$ 1724 (OAc), 1712 cm.$^{-1}$ (C=O) in KBr (Found: C, 65·1; H, 5·8. $C_{18}H_{19}O_5N$ requires C, 65·6; H, 5·8%). The second benzene eluate gave 1-O-*acetyl-β-dihydrolycorinone* (VI) (450 mg.), needles (from propan-2-ol), m. p. 200° (depressed the m. p. of the α-isomer to 185°), $[\alpha]_D$ −84·3° (*c* 0·59 in $CHCl_3$), $\lambda_{max.}$ 236 and 292 mμ (log ε 3·50 and 3·60), $\nu_{max.}$ 1739 (OAc) and 1715 cm.$^{-1}$ (C=O) in KBr (Found: C, 64·7; H, 5·9. $C_{18}H_{19}O_5N,\frac{1}{2}H_2O$ requires C, 64·5; H, 5·9%).

Reduction of 1-O-*Acetyl-β-dihydrolycorinone.*—(*a*) 1-*O*-Acetyl-β-dihydrolycorinone (VI) (20 mg.) and lithium aluminium hydride (30 mg.) in dry tetrahydrofuran (10 ml.) were kept at room temperature for 20 min., then heated under reflux for a further 20 min. After cooling, the excess of the reagent was destroyed with a little water, and the whole filtered; the filtrate afforded a residue which when crystallised from acetone gave β-dihydro-2-epilycorine (VIII; R = R′ = H), m. p. and mixed m. p. 145°.

(*b*) 1-*O*-Acetyl-β-dihydrolycorinone (150 mg.) was hydrogenated in acetic acid (30 mg.) with Adams catalyst (50 mg.) for 1 hr. The catalyst was removed and the mixture concentrated under reduced pressure, basified with aqueous ammonia, and extracted with chloroform. Evaporation of the chloroform afforded 1-O-*acetyl-β-dihydro-2-epilycorine* (VIII; R = Ac, R′ = H) (100 mg.), needles (from ethyl methyl ketone), m. p. 193—194°, $[\alpha]_D$ −142·6° (*c* 0·55 in $CHCl_3$), $\nu_{max.}$ 3367 (OH), 1718 cm.$^{-1}$ (OAc) (Found: C, 65·2; H, 6·6. $C_{18}H_{21}O_5N$ requires C, 65·2; H, 6·4%).

β-Dihydro-2-epilycorine.—1-*O*-Acetyl-β-dihydro-2-epilycorine (VIII; R = Ac, R′ = H) (70

mg.) was refluxed in 5% ethanolic potassium hydroxide (10 ml.) for 30 min. Evaporation of the ethanol and extraction of the residue with chloroform gave β-dihydro-2-epilycorine (VIII; R = R′ = H) (50 mg.), identical with an authentic specimen in m. p., mixed m. p., and infrared spectrum.

Reduction of the Ketone (V) *by Lithium Aluminium Hydride.*—The ketone (V) (9 mg.) and lithium aluminium hydride (30 mg.) in dry tetrahydrofuran (10 ml.) were set aside at room temperature for 20 min., then refluxed for further 20 min. Working up gave α-dihydro-2-epilycorine (VII; R = R′ = H) (3 mg.), m. p. and mixed m. p. 196—197°.

1-O-*Acetyldihydrolycorine from* 1-O-*Acetyl-lycorine.*—1-*O*-Acetyl-lycorine (300 mg.) and 10% palladium–carbon (400 mg.) in alcohol (30 ml.) were stirred in hydrogen for 3 hr. After working up in the usual manner, 1-*O*-acetyldihydrolycorine (III; R = Ac) (250 mg.), m. p. and mixed m. p. 199—200°, was obtained. Hydrolysis of this in boiling 10% alcoholic potassium hydroxide for 30 min. yielded dihydrolycorine, m. p. 255°, identical with the hydrogenation product of lycorine.

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758. *Stereochemistry of Lycorenine, Homolycorine, Pluviine, and their Hydrogenation Products.*

By Tsunehiro Kitagawa, Shojiro Uyeo, and Naokata Yokoyama.

The hydrogenation products of the alkaloids, lycorenine, homolycorine, and pluviine have been interrelated chemically and their steric structures elucidated. The absolute configurations of these alkaloids are also discussed.

The structures of hippeastrine and tazettine have been confirmed by conversion into lycorine β-methiodide and epihæmanthamine methiodide, respectively.

Kondo and Ikeda,[1,2] studying the hydrogenation of lycorenine, $C_{18}H_{23}O_4N$ (II; R = OH), an alkaloid isolated from bulbs of *Lycoris radiata* of the *Amaryllidaceae*, concluded that with Adams catalyst in acetic acid it gave two epimeric products, $C_{18}H_{25}O_3N$, which they called lævorotatory and dextrorotatory " desoxydihydro-R-lycorenine," where R denoted formation of a new ring; when palladium–charcoal was used they obtained in addition a third base which they named " desoxydihydrolycorenine; " this was assigned the formula, $C_{18}H_{25}O_3N,H_2O$, although the assumed water of crystallisation could not be removed even under drastic conditions.

Since both lævorotatory and dextrorotatory " desoxydihydro-R-lycorenines " were also obtained by hydrogenation of deoxylycorenine, which was originally obtained by electrolytic reduction [2] of lycorenine and later shown to be identical with anhydrotetrahydrohomolycorine [3] (II; R = H), they must be represented by the formulæ (I and III; R = H_2; or *vice versa*). Accordingly the lævorotatory and the dextrorotatory bases are now renamed α- and β-deoxydihydrolycorenine,* respectively.

On hydrogenation of *O*-acetyl-lycorenine, on the other hand, Kondo and Ikeda [2] isolated exclusively a product designated " acetyldesoxydihydrolycorenine," $C_{18}H_{21}O_3NAc,H_2O$, which gave on alkaline hydrolysis the above mentioned " desoxydihydrolycorenine."

* It will be shown that the compounds of the α-series have a *cis*-fused perhydroindole ring system as in α-dihydrocaranine, and those of the β-series a *trans*-fused one as in β-dihydrocaranine. In view of this, it is preferable to change the prefix α in dihydro-α-deoxylycorenine used provisionally [4] for the dextrorotatory base to β, as here.

[1] Kondo and Ikeda, *Ber.*, 1940, **73**, 867.
[2] Kondo and Ikeda, *Ann. Report ITSUU Lab.*, 1952, **3**, 55.
[3] Kitagawa, Taylor, Uyeo, and Yajima, *J.*, 1955, 1066.
[4] Uyeo and Yajima, *J.*, 1955, 3392.

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" Acetyldesoxydihydrolycorenine " and " desoxydihydrolycorenine " can now be formulated, in accord with the structure of *O*-acetyl-lycorenine (V; R = CHO, R′ = Ac), as (IV or VII; R = CH_2·OH, R′ = OAc, R″ = H) and (IV or VII; R = CH_2·OH, R′ = OH, R″ = H), respectively. In confirmation, tetrahydrohomolycorine (V; R = CH_2·OH, R′ = H) gave as the only isolatable hydrogenation product the expected hexahydrohomolycorine which was identical with Kondo's " desoxydihydrolycorenine." Since the hexahydrohomolycorine was convertible by acid into α-deoxydihydrolycorenine (I; R = H_2), it seemed preferable to rename Kondo's " acetyldesoxydihydrolycorenine " and " desoxydihydrolycorenine " as α-*O*-acetylhexahydrohomolycorine (IV; R = CH_2·OH, R′ = OAc, R″ = H) and α-hexahydrohomolycorine (IV; R = CH_2·OH, R′ = OH, R″ = H) respectively.

Hydrogenation of di-*O*-acetyltetrahydrohomolycorine (V; R = CH_2·OAc, R′ = Ac) gave, as was the case with acetyl-lycorenine, exclusively α-di-*O*-acetylhexahydrohomolycorine (IV; R = CH_2·OAc, R′ = OAc, R″ = H), identical with the product of acetylation of α-hexahydrohomolycorine (IV; R = CH_2·OH, R′ = OH, R″ = H). The same diacetate was also obtained by acetolysis of α-deoxydihydrolycorenine (I; R = H_2), although Kondo and Ikeda reported the isolation of the monoacetyl derivative (IV; R = CH_2·OH, R′ = OAc, R″ = H), identical with the product of hydrogenation of *O*-acetyl-lycorenine, probably owing to partial hydrolysis during their working up of the diacetate originally formed.

Reinvestigation of the acetolysis of β-deoxydihydrolycorenine (III; R = H_2) yielded the product obtained by Kondo and Ikeda who assigned to it the molecular formula $C_{20}H_{27}O_4N,H_2O$ containing one acetyl group. Our analytical values were, however, in accord with the formula, $C_{22}H_{31}O_6N$, containing two acetyl groups. Alkaline hydrolysis of the acetate, β-di-*O*-acetylhexahydrohomolycorine (VII; R = CH_2·OAc, R′ = OAc, R″ = H) afforded β-hexahydrohomolycorine (VII; R = CH_2·OH, R′ = OH, R″ = H), which reverted to β-deoxydihydrolycorenine (III; R = H_2) on treatment with dilute sulphuric acid.

Boit, Paul, and Stender [5] reported previously that homolycorine, $C_{18}H_{21}O_4N$ (II; R = O), gave, on hydrogenation with Adams catalyst in ethanol, a dihydrohomolycorine, m. p. 188°, together with a tetrahydro-derivative, characterised only as its methiodide, m. p. 290—291°. We have shown, however, that hydrogenation of the alkaloid under the conditions similar to those used by Boit *et al.* yielded, as expected, a pair of diastereoisomeric products (I and III; R = O), $C_{18}H_{23}O_4N$, m. p. 188—189° and 158—159°, respectively, which were characterised also as their methiodides, m. ps. 245—246° and 292—293°. The former was probably identical with Boit's dihydrohomolycorine, and the latter with the tetrahydrohomolycorine of the German authors.

Treatment of the higher-melting dihydrohomolycorine with lithium aluminium hydride yielded α-hexahydrohomolycorine (IV; R = CH_2·OH, R′ = OH, R″ = H), whereas the lower-melting one gave β-hexahydrohomolycorine (VII; R = CH_2·OH, R′ = OH, R″ = H). Thus the stereochemical relation between two pairs of hydrogenation products of lycorenine and homolycorine has been established, and it would be appropriate to give the revised names, α- and β-dihydrohomolycorine, to Boit's dihydrohomolycorine and tetrahydrohomolycorine, respectively.

In order to relate the structure and configuration of lycorenine or homolycorine to those of pluviine [6] (XIII), we converted tetrahydrohomolycorine (V; R = CH_2·OH, R′ = H) into pluviine as follows. Tetrahydrohomolycorine with toluene-*p*-sulphonyl chloride in pyridine furnished a quaternary salt, isolated as its crystalline iodide, m. p. 232—233°, diastereoisomeric with the known pluviine methiodide (IX), m. p. 259—261°, since pyrolysis of the corresponding methochloride afforded pluviine and anhydromethylpseudolycorine [6-8]

[5] Boit, Paul, and Stender, *Chem. Ber.*, 1955, **88**, 133.
[6] Boit, Ehmke, Uyeo, and Yajima, *ibid.*, 1957, **90**, 363.
[7] Uyeo and Yanaihara, *J.*, 1959, 172.
[8] Fales, Giuffrida, and Wildman, *J. Amer. Chem. Soc.*, 1956, **78**, 4145.

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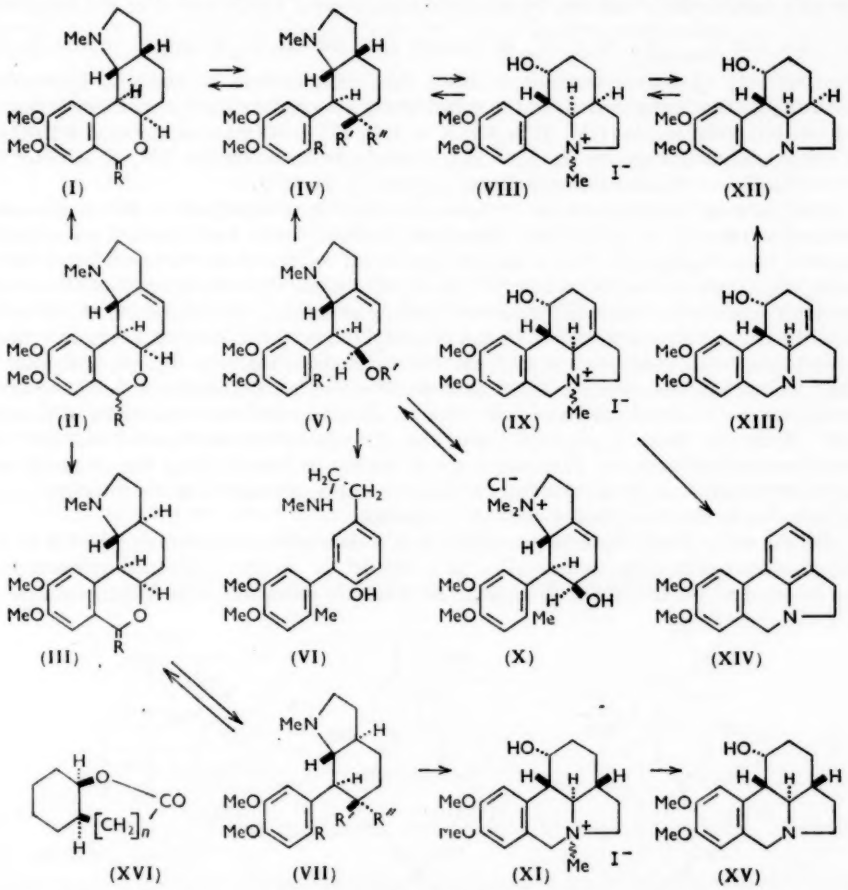
(XIV). In this pyrolysis, the possibility of change in structure or configuration other than that at the nitrogen atom was highly improbable, since we have demonstrated that the model compound (V; R = Me, R′ = H), obtained previously by Wolff–Kishner reduction of lycorenine [4] and now named deoxolycorenine, was regenerated from its methochloride (X) by distillation in a high vacuum.

The methiodide, m. p. 259—261°, is now designated pluviine α-methiodide and its diastereoisomer, m. p. 232—233°, pluviine β-methiodide; isomeric pairs have been noted



previously in this series, *e.g.*, lycorine α- and β-methiodide [9] and caranine α- and β-methiodide.[10] This view was confirmed by conversion of α- and β-hexahydrohomolycorine (IV and VII; R = CH_2·OH, R′ = OH, R″ = H) into the corresponding dihydropluviines (XII and XV). Thus α-hexahydrohomolycorine with toluene-*p*-sulphonyl chloride in pyridine, as above, gave α-dihydropluviine β-methiodide, which was obtained with its α-isomer by quaternisation with methyl iodide of α-dihydropluviine which was in turn prepared by hydrogenation of pluviine with Adams catalyst in acetic acid.

Vacuum-pyrolysis of α-dihydropluviine β-methiodide afforded, in a low yield, α-dihydropluviine (XII). From β-hexahydrohomolycorine we obtained by a similar

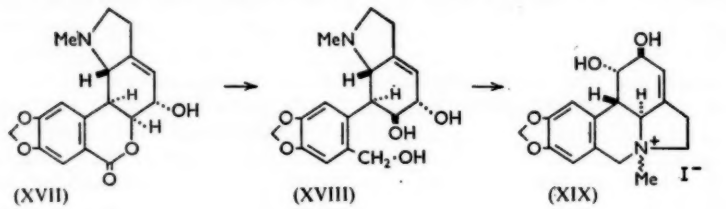
[9] Kondo, Katsura, and Uyeo, *Ber.*, 1938, **71**, 1529.
[10] Warnhoff and Wildman, *J. Amer. Chem. Soc.*, 1957, **79**, 2192.

sequence of reactions a base indistinguishable from the β-dihydropluviine (XV) which was formed by hydrogenation of pluviine in ethanol in the presence of palladium–charcoal.

Emde degradation of pluviine β-methiodide furnished deoxolycorenine (V; R = Me, R′ = H); likewise α-dihydropluviine β-methiodide afforded a base, named α-deoxodihydrolycorenine (IV; R = Me, R′ = OH, R″ = H), identical with the sole product obtained by the hydrogenation of deoxolycorenine with Adams catalyst in acetic acid. Since deoxolycorenine was obtained from lycorenine not only by Wolff–Kishner method but also under mild conditions by desulphurisation with Raney nickel of the thioacetal (V; R = $CH\langle^{S-CH_2}_{S-CH_2}$, R′ = H), it appears that all the bonds linked to the hydroaromatic ring of deoxolycorenine retained the configurations of those in lycorenine. Accordingly, the configurations of the substituents attached to the hydroaromatic ring of α-deoxodihydrolycorenine (IV; R = Me, R′ = OH, R″ = H) must be identical with those of α-deoxydihydrolycorenine (I; R = H_2), α-hexahydrohomolycorine (IV; R = CH_2·OH, R′ = OH, R″ = H), and α-dihydrohomolycorine (I; R = O).

In an attempt to determine the configuration of the hydroxyl group in deoxolycorenine, we have oxidised it by a modified Oppenauer method [11] and have isolated an optically inactive base, $C_{18}H_{23}O_3N$, whose infrared spectrum exhibited no carbonyl band but a strong absorption in the OH and/or NH stretching region, while the ultraviolet absorption spectrum suggested a somewhat hindered diphenyl grouping. Acetylation of this product yielded a neutral oil which showed *O*- and *N*-acetyl bands in the infrared spectrum. With methyl iodide in acetone it gave an *N*-methyl methiodide, and with dimethyl sulphate in alkali followed by potassium iodide it gave an *ON*-dimethyl methiodide which in contrast to the starting material gave no colour with an alkaline solution of diazotised sulphanilic acid. Thus the base, $C_{18}H_{23}O_3N$, must be 2′-hydroxy-4,5-dimethoxy-2-methyl-5′-(2-methylaminoethyl)biphenyl (VI) which could readily be formed from the originally expected cyclohexenone by elimination of nitrogen and isomerisation of the resulting cyclohexadienone to the energetically more stable phenol.

On the other hand, Oppenauer oxidation of α-deoxodihydrolycorenine yielded as expected, α-deoxodihydrolycorenone (IV; R = Me, R′, R″ = O). α-Deoxodihydrolycorenone reverted to α-deoxodihydrolycorenine on catalytic reduction with Adams catalyst in



acetic acid, while with lithium aluminium hydride or sodium borohydride it was reduced to an epimer, α-deoxodihydroepilycorenine (IV; R = Me, R′ = H, R″ = OH). Since catalytic hydrogenation of cyclohexanones in acid solution usually gives axial hydroxy-compounds and metal-hydride reduction equatorial ones, we assigned to the hydroxyl

[11] Woodward, Wendler, and Brutschy, *J. Amer. Chem. Soc.*, 1945, **67**, 1425.

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group in α-deoxodihydrolycorenine the axial conformation and to that in its epimer the equatorial conformation. Accordingly, the benzene ring linked to the hydroaromatic ring in lycorenine or homolycorine must be equatorial, since the oxygen atom linked to the cyclohexene ring of the respective alkaloids must be axial, as is that of α-deoxodihydrolycorenine, and *trans*-fusion of two six-membered rings through two vicinal axial linkages is sterically impossible. The C–N bond on the cyclohexene ring in lycorenine or homolycorine must be equatorial, otherwise a pair of diastereoisomeric dihydro-derivatives of deoxylycorenine or homolycorine cannot be produced by saturation of the ethylenic bond in the respective molecules. Thus lycorenine and homolycorine must have the structures and configurations shown in (II; R = OH and O, respectively). Moreover, the steric structure of pluviine can be represented by the formula (XIII), if we exclude the most unlikely possibility of stereochemical change during conversion of tetrahydrohomolycorine into pluviine.

The structure and configuration of pluviine thus deduced are identical with those of caranine [10,12] except for the difference between two methoxyl groups and a methylenedioxy-group. Thus the stereochemical behaviour of the two alkaloids toward hydrogenation ought to be very similar. Since both α- and β-dihydropluviine were prepared from pluviine under the conditions used for the preparation of α- and β-dihydrocaranine [10] from caranine, it followed that the configurations of the former pair must be comparable with those of the latter which have been elucidated by Takeda and Kotera.[13] α- and β-Dihydropluviine can be represented, therefore, by (XII) and (XV), respectively.

As to the absolute configuration of lycorenine, homolycorine, and pluviine, strong evidence can be gained from molecular-rotation considerations. According to the Hudson's lactone rule extended by Klyne,[14] lactones of the general formula (XVI) are more positive in molecular rotation that the corresponding hydroxy-acids or their equivalents. If we can apply the rule to homolycorine and related compounds containing six-membered lactone rings, all the values given in the annexed Table are consistent with the assumption that homolycorine has the absolute configuration represented by the formula (II; R = O).

Consequently lycorenine and pluviine have absolute configurations (II; R = OH) and

Molecular rotations of homolycorine and related compounds.

Compound	$[M]_D$	$\Delta[M]_D$
Homolycorine	+268°	
Tetrahydrohomolycorine	−322	+590°
Deoxolycorenine	−445	+713
Lycorenine oxime	−542	+810
α-Dihydrohomolycorine	−164	
α-Hexahydrohomolycorine	−234	+70
α-Deoxodihydrolycorenine	−170	+6
β-Dihydrohomolycorine	−85	
β-Hexahydrohomolycorine	−143	+58

(XIII), respectively, which are comparable with those of lycorine and caranine, reported in the preceding paper.[15]

In connection with the studies mentioned above, we have converted hippeastrine [16] and tazettine,[17,18] two alkaloids of the *Amaryllidaceae*, into lycorine and epihæmanthamine methiodide, respectively.

For hippeastrine, $C_{17}H_{17}O_5N$, Boit [16] proposed structure (XVII), in analogy with homolycorine, since it contains a δ-lactone along with a methylenedioxy- and an acetylatable hydroxy-group. To prove this structure, we treated tetrahydrohippeastrine (XVIII),

[12] Takeda, Kotera, and Mizukami, *J. Amer. Chem. Soc.*, 1958, **80**, 2562.
[13] Takeda and Kotera, *Chem. and Ind.*, 1956, 347; *Pharm. Bull. (Japan)*, 1957, **5**, 234.
[14] Klyne, *Chem. and Ind.*, 1954, 1198.
[15] Nakagawa and Uyeo, preceding paper.
[16] Boit, *Chem. Ber.*, 1956, **89**, 1129, 2093, 2462.
[17] Ikeda, Taylor, Tsuda, Uyeo, and Yajima, *J.*, 1956, 4749.
[18] Irie, Tsuda, and Uyeo, *J.*, 1959, 1446.

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the product of reduction of hippeastrine with lithium aluminium hydride, with toluene-*p*-sulphonyl chloride in pyridine as in the conversion of homolycorine into pluviine β-methiodide: we obtained lycorine β-methiodide (XIX). Since the structure and absolute configuration of lycorine [15] have been firmly established, hippeastrine is represented by the formula (XVII).

As reported in a previous paper,[17] tazettine (XX) can be converted into tazettadiol (XXI) which appeared to serve as a useful precursor to the hæmanthamine ring system.[19] An attempt was therefore made, but without success, to convert tazettadiol into hæmanthamine methiodide or a stereoisomer by toluene-*p*-sulphonyl chloride and pyridine as above. On the other hand, thionyl chloride in pyridine was found suitable as a reagent to quaternise the nitrogen atom of tazettadiol with the benzyl group in the same molecule. The product thus obtained in a good yield was shown to be identical with epihæmanthamine methiodide (XXII) in which the secondary hydroxyl group is epimeric with that of hæmanthamine.

Experimental

Ultraviolet absorption spectra were determined for 95% EtOH solutions, rotations are for EtOH solutions, and infrared spectra refer to Nujol mulls unless otherwise stated. The light petroleum used had b. p. 45—65°.

Hydrogenation of Lycorenine.—Catalytic hydrogenation of lycorenine (1 g.) with Adams catalyst (0·3 g.) in acetic acid (10 ml.) was carried out as described by Kondo and Ikeda.[2] The products were separated by chromatography in benzene–light petroleum (1 : 2) over alumina, yielding from the first fractions α-deoxydihydrolycorenine (0·3 g.), needles (from methanol), m. p. 127—128°, $[\alpha]_D$ −15·3° (*c* 1·5), $\lambda_{max.}$ 285 mμ (log ε 3·55) (Found: C, 70·8; H, 8·2. Calc. for $C_{18}H_{25}O_3N$: C, 71·3; H, 8·3%), and from the second fractions β-deoxydihydrolycorenine (0·35 g.), needles (from acetone), m. p. 168—169°, $[\alpha]_D$ +19·9° (*c* 0·3), $\lambda_{max.}$ 285 mμ (log ε 3·55) (Found: C, 71·6; H, 8·2%).

α-*Hexahydrohomolycorine* (IV; R = CH_2·OH, R′ = OH, R″ = H).—Tetrahydrohomolycorine (0·5 g.) in acetic acid (15 ml.) was shaken with Adams catalyst (0·1 g.) in hydrogen for 5 hr. Evaporation of the filtered solution *in vacuo* and isolation of the product with ether after basification with aqueous ammonia yielded α-hexahydrohomolycorine (0·45 g.), plates (from acetone), m. p. 175—176°, $[\alpha]_D$ −73·0° (*c* 0·6), $\lambda_{max.}$ 281 mμ (log ε 3·45) (Found: C, 67·3; H, 8·2. Calc. for $C_{18}H_{27}O_4N$: C, 67·3; H, 8·5%), identical in m. p. and mixed m. p. with Kondo's desoxydihydrolycorenine.[2]

α-*Di*-O-*acetylhexahydrohomolycorine* (IV; R = CH_2·OAc, R′ = OAc, R″ = H).—(*a*) Di-*O*-acetyltetrahydrohomolycorine [3] (0·61 g.) in acetic acid (20 ml.) was hydrogenated over Adams catalyst (0·11 g.) for 5 hr. Working up in the usual manner and crystallisation from ether gave α-*di*-O-*acetylhexahydrohomolycorine* (0·6 g.), as needles, m. p. 101—102°, $[\alpha]_D$ −34·5° (*c* 0·55), $\lambda_{max.}$ 281 mμ (log ε 3·43), $\nu_{max.}$ 1733 cm.$^{-1}$ (Found: C, 65·4; H, 7·7; N, 3·8; Ac, 20·9. $C_{22}H_{31}O_6N$ requires C, 65·2; H, 7·7; N, 3·5; 2Ac, 21·2%).

(*b*) α-Deoxydihydrolycorenine (0·11 g.) was kept in acetic anhydride (6 ml.) and sulphuric acid (0·1 ml.) at room temperature overnight. After addition of water (10 ml.), the mixture was basified with aqueous ammonia and extracted with chloroform. Evaporation of the extract gave a residue (55 mg.) which was filtered through alumina (1 g.) in benzene to furnish α-di-*O*-acetylhexahydrohomolycorine, m. p. and mixed m. p. 101—102°.

(*c*) α-Hexahydrohomolycorine (50 mg.) in acetic anhydride (3 ml.) containing sulphuric acid (0·1 ml.) was set aside at room temperature for 24 hr. The acetic anhydride was decomposed with water, and the mixture basified with aqueous sodium carbonate and extracted with ether, to give α-di-*O*-acetylhexahydrohomolycorine (25 mg.), m. p. and mixed m. p. 101—102°.

(*d*) α-*O*-Acetylhexahydrohomolycorine [2] (50 mg.) obtained by hydrogenation of *O*-acetyllycorenine was treated with acetic anhydride (3 ml.) containing sulphuric acid (0·1 ml.) at room temperature for 24 hr. The resulting acetate (30 mg.) was identical with α-di-*O*-acetylhexahydrohomolycorine obtained as above.

β-*Diacetylhexahydrohomolycorine* (VII; R = CH_2·OAc, R′ = OAc, R″ = H).—β-Deoxydihydrolycorenine (0·12 g.) was heated in acetic anhydride (3 ml.) at 50—55° for 1·5 hr. After dilution with water, the mixture was basified with aqueous ammonia and extracted with ether.

[19] Fales and Wildman, *Chem. and Ind.*, 1958, 561.

The extract gave on concentration β-di-*O*-acetylhexahydrohomolycorine (90 mg.) as prisms (from ether–light petroleum), m. p. 122—123°, $[\alpha]_D$ −36·5° (*c* 0·5), $\lambda_{max.}$ 281 mμ (log ε 3·42), $\nu_{max.}$ 1737, 1724 cm.$^{-1}$ (OAc) (Found: C, 65·5; H, 7·7; Ac, 20·6%), identical with Kondo and Ikeda's sample obtained by the same procedure.[2]

β-Hexahydrohomolycorine (VII; R = CH_2·OH, R′ = OH, R″ = H).—β-Di-*O*-acetylhexahydrohomolycorine (40 mg.) and potassium hydroxide (1 g.) were refluxed in methanol (10 ml.) for 2 hr. Isolation of the product in the usual manner and crystallisation from acetone gave *β-hexahydrohomolycorine* (30 mg.) as prisms, m. p. 165°, $[\alpha]_D$ −44·5° (*c* 0·83), $\lambda_{max.}$ 281 mμ (log ε 3·45) (Found: C, 67·3; H, 8·4; N, 4·4. $C_{18}H_{27}O_4N$ requires C, 67·3; H, 8·5; N, 4·4%).

Heating this (50 mg.) in 5% aqueous sulphuric acid (5 ml.) on a water-bath for 2 hr. converted it into β-deoxydihydrolycorenine (35 mg.), m. p. and mixed m. p. 168—169°.

Hydrogenation of Homolycorine.—Homolycorine (1·1 g.) in ethanol (30 ml.) was shaken with Adams catalyst (0·3 g.) in hydrogen for 5 hr. Evaporation of the filtered solution and crystallisation from acetone afforded α-dihydrohomolycorine (0·33 g.) as plates, m. p. 188–189°, $[\alpha]_D$ −51·9° (*c* 0·65), $\lambda_{max.}$ 226, 267, and 302 mμ (log ε 4·32, 3·92, and 3·70), $\nu_{max.}$ 1698 cm.$^{-1}$ (lactone) (Found: C, 67·9; H, 7·3; N, 4·3. Calc. for $C_{18}H_{23}O_4N$: C, 68·1; H, 7·3; N, 4·4%). The methiodide formed plates (from ethanol), m. p. 245—246° (decomp.), $[\alpha]_D$ −10·8° (*c* 0·37 in 50% aqueous EtOH). The methopicrate had m. p. 218° (decomp.) (from methanol).

The mother-liquors from α-dihydrohomolycorine were combined and evaporated to dryness, and the residue was dissolved in ether. The material remaining undissolved gave, on crystallisation from acetone, an additional crop (50 mg.) of α-dihydrohomolycorine. Concentration of the ethereal solution and crystallisation from ether gave *β-dihydrohomolycorine* (0·35 g.) as plates, m. p. 158—159°, $[\alpha]_D$ −26·9° (*c* 0·85), $\lambda_{max.}$ 227, 268, and 303 mμ (log ε 4·32, 3·91, and 3·69), $\nu_{max.}$ 1715 cm.$^{-1}$ (lactone) (Found: C, 67·9; H, 7·2; N, 4·1%). The methiodide formed long prisms (from methanol), m. p. 292—293° (decomp.), $[\alpha]_D$ −25·3° (*c* 0·35 in 50% aqueous EtOH). The *methopicrate* had m. p. 241—242° (decomp.) (from methanol) (Found: C, 53·2; H, 5·1; N, 10·0. $C_{25}H_{28}O_{11}N_4$ requires C, 53·6; H, 5·1; N, 10·0%).

Reduction of α- and β-Dihydrohomolycorine by Lithium Aluminium Hydride.—α-Dihydrohomolycorine (70 mg.) and lithium aluminium hydride (100 mg.) were refluxed in dry ether (30 ml.) for 5 hr. After addition of moist ether and filtration of the precipitate, the filtrate and washings were combined and evaporated, to give α-hexahydrohomolycorine (50 mg.), m. p. and mixed m. p. 175—176°.

In a similar way, β-dihydrohomolycorine (80 mg.) was converted into β-hexahydrohomolycorine (30 mg.), m. p. and mixed m. p. 165°.

Conversion of Tetrahydrohomolycorine into Pluviine β-Methiodide.—Toluene-*p*-sulphonyl chloride (1·15 g.) was added to a solution of tetrahydrohomolycorine (1·6 g.) in dry pyridine (20 ml.), and the whole set aside at room temperature overnight. The mixture was evaporated to dryness under reduced pressure, and the residue passed in water through a column of Amberlite I.R.A.-400 resin (OH-form). The column was washed with water, and the combined eluate and washings were washed with ether several times to remove pyridine, then acidified with dilute hydriodic acid, filtered, and concentrated under reduced pressure, yielding *pluviine β-methiodide*, which on crystallisation from methanol formed prisms (0·98 g.), m. p. 231—232°, $[\alpha]_D$ +38·2° (*c* 0·9 in H_2O) (Found: C, 50·6; H, 5·5; N, 3·4. $C_{18}H_{24}O_5NI$ requires C, 50·4; H, 5·6; N, 3·3%). The *methopicrate* prepared in water formed yellow prisms (from ethanol), m. p. 234—235° (Found: C, 54·5; H, 5·0; N, 10·6. $C_{24}H_{26}O_{10}N_4$ requires C, 54·5; H, 4·9; N, 10·6%).

For comparison, *pluviine α-methopicrate* was prepared from pluviine α-methiodide and picric acid in hot water, forming scales, m. p. 169—171° (from ethanol) (Found: C, 54·5; H, 4·9; N, 10·7%).

The *β-methotoluene-*p*-sulphonate* was prepared by passage of an aqueous solution of the β-methiodide through a column of Amberlite I.R.A-400 resin (OH-form) followed by neutralisation of the eluate and washings with toluene-*p*-sulphonic acid and concentration to dryness. Recrystallisation from acetone–ethanol gave prisms, m. p. 198—200° (Found: C, 63·6; H, 6·5; N, 2·9. $C_{25}H_{31}O_6NS$ requires C, 63·4; H, 6·6; N, 3·0%).

Vacuum-pyrolysis of Pluviine β-Methochloride.—Pluviine β-methiodide (0·8 g.) was converted into its methochloride by shaking its aqueous solution with an excess of silver chloride. The filtered solution was evaporated to dryness under reduced pressure and the resulting chloride (0·6 g.) immediately distilled at 220—260° (bath)/0·01—0·005 mm. The distillate (0·25 g.) was taken up in dilute hydrochloric acid, washed with ether, basified with aqueous ammonia,

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and extracted with chloroform. Evaporation of the chloroform left a residue which was chromatographed in benzene over alumina. Elution with benzene afforded anhydromethylpseudolycorine (60 mg.), needles (from methanol), m. p. and mixed m. p. 174—176° (Found: C, 76·1; H, 6·4; N, 5·3. Calc. for $C_{17}H_{17}O_2N$: C, 76·4; H, 6·4; N, 5·2%). Elution with chloroform yielded pluviine (80 mg.), m. p. and mixed m. p. 224—226° (from methanol), $[\alpha]_D$ −146·3° (*c* 0·8) (Found: C, 71·0; H, 7·2; N, 5·0. Calc. for $C_{17}H_{21}O_3N$: C, 71·1; H, 7·4; N, 4·9%). The infrared spectrum was identical with that of authentic pluviine.

α-Dihydropluviine.—Pluviine (0·26 g.) in acetic acid (20 ml.) was shaken in hydrogen in the presence of Adams catalyst (40 mg.) for 30 min. Evaporation of the filtered solution under reduced pressure yielded a residue which was taken up in 3% aqueous hydrochloric acid, washed with benzene, basified with aqueous ammonia, and extracted with benzene. Concentration of the benzene gave *α-dihydropluviine* which on crystallisation from acetone formed needles, m. p. 130—133°, or cubes, m. p. 136—139° (dimorphous, since they were interconvertible on seeding of a concentrated solution of one form in acetone with the other), $[\alpha]_D$ −87·2° (*c* 0·92), $\lambda_{max.}$ 232 and 282 mμ (log ε 3·88 and 3·55) (Found: C, 70·6; H, 8·0; N, 4·8. $C_{17}H_{23}O_3N$ requires C, 70·6; H, 8·0; N, 4·8%).

α-Dihydropluviine α- and β-Methiodide.—α-Dihydropluviine (82 mg.) was heated in methanol (1 ml.) with methyl iodide (0·5 ml.) on the water-bath for 4 hr. The mixture was evaporated to dryness and the residue crystallised from ethanol, to give *α-dihydropluviine α-methiodide* (40 mg.) as needles, m. p. 219—221°, raised to 223—224° on repeated crystallisations, $[\alpha]_D$ −74·4° (*c* 1·0 in H_2O) (Found: C, 49·3; H, 6·2. $C_{18}H_{26}O_3NI,\frac{1}{2}H_2O$ requires C, 49·1, H, 6·1%).

The mother-liquors from the crystallisations of the α-methiodide were evaporated to dryness and passed in acetone through a column of alumina. Elution with acetone yielded *α-dihydropluviine β-methiodide* (60 mg.) which formed prisms (from ethanol), m. p. 136—139°, raised on drying *in vacuo* to 231—233°, $[\alpha]_D$ −43·2° (*c* 0·92 in H_2O) [Found, for a sample (m. p. 136—139°): C, 48·2; H, 6·2. $C_{18}H_{26}O_3NI,H_2O$ requires C, 48·1; H, 6·2%. Found, for a sample dried *in vacuo* (m. p. 231—233°): C, 48·8; H, 6·1. $C_{18}H_{26}O_3NI,\frac{1}{2}H_2O$ requires C, 49·1; H, 6·1%]. The m. p. was depressed on admixture with α-dihydropluviine α-methiodide and the infrared spectrum was not identical with that of the latter.

α-Dihydropluviine β-Methiodide from α-Hexahydrohomolycorine.—α-Hexahydrohomolycorine (0·3 g.) and toluene-*p*-sulphonyl chloride (0·23 g.) in dry pyridine (10 ml.) were kept at room temperature overnight. The mixture was evaporated to dryness under reduced pressure and the residue, dissolved in water, was passed through a column of Amberlite I.R.A.-400 resin (OH-form). The combined eluate and washings were washed repeatedly with ether to remove pyridine and then neutralised with hydriodic acid. The solution was filtered, evaporated to dryness, and crystallised from chloroform and ethanol, to give α-dihydropluviine β-methiodide as prisms, m. p. and mixed m. p. 231—233° (after drying *in vacuo*), $[\alpha]_D$ −45·5° (*c* 0·8 in H_2O) (Found: C, 49·7; H, 6·2. Calc. for $C_{18}H_{26}O_3NI,\frac{1}{2}H_2O$: C, 49·1; H, 6·1%). The infrared spectrum was identical with that of the same compound derived from α-dihydropluviine.

Vacuum-pyrolysis of α-Dihydropluviine β-Methochloride.—α-Dihydropluviine β-methiodide (0·1 g.) in methanol was shaken with freshly prepared silver chloride. After removal of the silver salts, the solution was evaporated to dryness and distilled at 200—260°/0·01—0·002 mm. The distillate, dissolved in chloroform, was extracted with 3% hydrochloric acid, and the aqueous layer was washed with ether, basified with aqueous ammonia, and extracted with chloroform. The chloroform was removed and the residue (10 mg.) passed in benzene through alumina. The column was washed with benzene and benzene–chloroform (9 : 1) and eluted with chloroform. The concentrated eluate was crystallised from acetone, giving α-dihydropluviine as prisms (3 mg.), m. p. and mixed m. p. 137—138°.

β-Dihydropluviine.—Pluviine (40 mg.) was hydrogenated in ethanol (10 ml.) with 2·5% palladium–charcoal (0·2 g.) for 1 hr. After isolation in the usual way, the product was chromatographed in benzene over alumina. Elutions with benzene and benzene–chloroform (9 : 1) gave no crystalline substance. Elution with chloroform yielded *β-dihydropluviine* (20 mg.) as prisms, m. p. 176—178° (from acetone), $[\alpha]_D$ −168° (*c* 0·8) (Found: C, 70·2; H, 8·1; N, 5·1. $C_{17}H_{23}O_3N$ requires C, 70·6; H, 8·0; N, 4·8%). This was not identical with α-dihydropluviine in mixed m. p. and infrared spectrum.

β-Dihydropluviine from β-Hexahydrohomolycorine.—β-Hexahydrohomolycorine (0·3 g.) and toluene-*p*-sulphonyl chloride (0·23 g.) were allowed to react in pyridine (10 ml.) as for tetrahydrohomolycorine. After working up, *β-dihydropluviine methiodide* (0·12 g.) crystallised

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from methanol in prisms, m. p. 265—267°, $[\alpha]_D$ −30·7° (*c* 0·62 in H_2O) (Found: C, 50·0; H, 6·1; N, 3·2. $C_{18}H_{26}O_3NI$ requires C, 50·1; H, 6·1; N, 3·3%).

β-Pluviine methiodide (0·1 g.) thus obtained was converted into its chloride in the usual way and distilled at 200—240°/0·01—0·002 mm., to give a distillate which was dissolved in benzene and passed through alumina. A chloroform eluate afforded prisms (4 mg.), m. p. 169—173°, identified as β-dihydropluviine by m. p. and mixed m. p.

Deoxolycorenine (V; R = Me, R′ = H).—(*a*) A modified Wolff–Kishner reduction of lycorenine has been reported earlier,[4] but the following mild conditions gave a better yield of the product.

Lycorenine (1 g.), 100% hydrazine hydrate (10 ml.), and potassium hydroxide (7 g.) were heated in diethylene glycol (20 ml.) at 150—155° for 3 hr. Then water (40 ml.) was added and the mixture extracted with ether which was washed with water, dried, and evaporated to dryness, giving deoxolycorenine (850 mg.) (from ether–light petroleum), m. p. 128—129°.

(*b*) A mixture of lycorenine (1·1 g.), ethanedithiol (1·8 ml.), and boron trifluoride–ether complex (2 ml.) was heated on a water-bath for 10 min. After being kept at room temperature overnight, the mixture was concentrated under reduced pressure and the residue washed 3 times with ether and then crystallised from methanol, to give a lycorenine ethylene dithioacetal boron trifluoride complex (1·55 g.) as prisms, m. p. 230° (decomp.). A solution of the complex in methanol (5 ml.) and water (20 ml.) was basified with aqueous ammonia and extracted with chloroform which gave on evaporation *lycorenine ethylene dithioacetal* (1 g.), m. p. 168—169° (from ethanol), $[\alpha]_D$ +17·2° (*c* 1·1) (Found: C, 60·9; H, 6·8; N, 3·5. $C_{20}H_{27}O_3NS_2$ requires C, 61·1; H, 7·0; N, 3·6%).

The thioacetal (0·6 g.) and Raney nickel (2 g.) were refluxed in ethanol (30 ml.) for 5 hr. Evaporation of the filtered solution gave an oil (420 mg.) which was taken up in ether and converted into the picrate (310 mg.) with an excess of ethereal picric acid. Crystallisation of the precipitated picrate afforded α-deoxodihydrolycorenine picrate (see below), m. p. and mixed m. p. 231—232°.

An ethereal solution of the mother-liquor from the filtration of the picrate was washed with aqueous sodium hydroxide to remove the excess of reagent, dried, and evaporated to give an oil (0·17 g.), which was chromatographed in benzene over alumina (3 g.). A benzene eluate gave deoxolycorenine (80 mg.), m.p. 128—129° (from ether–light petroleum), identical in m. p. and mixed m. p. with a sample derived by the method (*a*) above.

Vacuum-pyrolysis of Deoxolycorenine Methochloride.—Deoxolycorenine (0·18 g.) and methyl iodide (1 g.) in methanol (3 ml.) were refluxed for 2 hr., to give the *methiodide* as plates (0·2 g.), m. p. 244° (decomp.) (from methanol) (Found: C, 51·2; H, 6·1; N, 3·3. $C_{19}H_{28}O_3NI$ requires C, 51·2; H, 6·3; N, 3·1%). The methiodide (0·2 g.) was shaken with silver chloride (2 g.) in 50% aqueous methanol (10 ml.) for 1 hr. Evaporation of the filtered solution to dryness and distillation of the residue in an oil-bath at 220—240°/0·01—0·005 mm. gave a sublimate (70 mg.) which crystallised on trituration with ether, to give deoxolycorenine, m. p. and mixed m. p. 128—129°.

Emde Degradation of Pluviine β-*Methiodide.*—Pluviine β-methochloride, prepared from pluviine β-methiodide (0·3 g.) and silver chloride, was dissolved in water (4 ml.) and heated with sodium amalgam (15 g.) on a water-bath for 10 hr. After cooling, the separated oil was taken up in ether which was washed with water, dried, and evaporated to an oil. Crystallisation from ether gave prisms (60 mg.), m. p. 126—127° alone or mixed with deoxolycorenine (Found: C, 71·4; H, 8·3; N, 4·7. Calc. for $C_{18}H_{25}O_3N$: C, 71·3; H, 8·3; N, 4·6%).

Emde Degradation of α-*Dihydropluviine* β-*Methiodide.*—α-Dihydropluviine β-methiodide (80 mg.) was subjected to the Emde degradation in a similar manner to that described for the degradation of pluviine β-methiodide. Crystallisation of the product from ether gave prisms (25 mg.), m. p. 98—99°, identical in m. p. and mixed m. p. with α-deoxodihydrolycorenine.

2′-Hydroxy-4,5-dimethoxy-2-methyl-5′-(2-methylaminoethyl)biphenyl (VI).—A solution of deoxolycorenine (0·3 g.), benzophenone (0·9 g.), and potassium t-butoxide (0·5 g.) in dry benzene (30 ml.) was refluxed for 6 hr. After cooling, the mixture was extracted with 5% hydrochloric acid, and the aqueous layer washed with ether, basified with aqueous ammonia, and extracted with ether. The ethereal extract gave on evaporation *2′-hydroxy-4,5-dimethoxy-2-methyl-5′-(2-methylaminoethyl)biphenyl* as prisms (0·2 g.) (from acetone), m. p. 133—134°, $[\alpha]_D$ 0 (*c* 1·3), $\lambda_{max.}$ 285 mμ (log ε 3·92), $\nu_{max.}$ 3300 cm.$^{-1}$ (OH and NH) (Found: C, 71·5; H, 7·7; N, 4·5. $C_{18}H_{23}O_3N$ requires C, 71·7; H, 7·7; N, 4·7%).

The biphenyl gave with acetic anhydride and sodium acetate an oily diacetate whose infrared spectrum showed carbonyl bands at 1757 (OAc) and 1639 cm.$^{-1}$ (NAc).

The N-*methyl methiodide* was prepared with methyl iodide in boiling acetone and formed prisms (from acetone), m. p. 228° (decomp.), $\lambda_{max.}$ 285 mμ (log ε 3·90) (Found: C, 52·6; H, 6·2. $C_{20}H_{28}O_3NI$ requires C, 52·5; H, 6·2%). The ON-*dimethyl methiodide* was obtained by the action of dimethyl sulphate in alkali followed by treatment with potassium iodide. It formed prisms (from acetone), m. p. 212—213° (decomp.), $\lambda_{max.}$ 285 mμ (log ε 3·90) (Found: C, 53·3; H, 6·3; N, 3·1; OMe, 19·4. $C_{21}H_{30}O_3NI$ requires C, 53·5: H, 6·4; N, 3·0; 3OMe, 19·7%).

α-*Deoxodihydrolycorenine* (IV; R = Me, R′ = OH, R″ = H).—Deoxolycorenine (1·7 g.) in acetic acid (20 ml.) was shaken in hydrogen in the presence of Adams catalyst (0·12 g.) for 3 hr. Working up in the usual manner gave α-*deoxodihydrolycorenine* (1·6 g.) as plates, m. p. 98° (from ether), $[\alpha]_D$ −55·3° (*c* 1·63) (Found: C, 70·4; H, 8·8; N, 4·3. $C_{18}H_{27}O_3N$ requires C, 70·8; H, 8·9; N, 4·6%). The *picrate* formed needles (from methanol), m. p. 232° (decomp.) (Found: C, 54·0; H, 5·8; N, 10·6. $C_{24}H_{30}O_{10}N_4$ requires C, 53·9; H, 5·7; N, 10·5%). The *methiodide* formed plates (from methanol), m. p. 216° (decomp.) (Found: C, 51·3; H, 7·0. $C_{19}H_{30}O_3NI$ requires C, 51·0; H, 6·8%).

α-*Deoxodihydrolycorenone* (IV; R = Me, R′, R″ = O).—A solution of deoxodihydrolycorenine (0·5 g.), benzophenone (1 g.), and potassium t-butoxide (0·7 g.) in dry benzene (50 ml.) was heated under reflux for 5 hr. After cooling, the mixture was extracted with 2% hydrochloric acid which was washed with ether, basified with aqueous ammonia, and extracted with ether. Evaporation of the ethereal extract yielded α-deoxodihydrolycorenone as an oil (0·4 g.) which was immediately converted into its *picrate* (0·55 g.), needles (from methanol), m. p. 148°, $\nu_{max.}$ 1727 cm.$^{-1}$ (CO) (Found: C, 54·0; H, 5·4; N, 10·6. $C_{24}H_{28}O_{10}N_4$ requires C, 54·1; H, 5·3; N, 10·5%). The base, regenerated by passing the picrate through alumina, is an oil, $[\alpha]_D$ +95·9° (*c* 0·83).

The *oxime hydrochloride* was prepared in the usual manner and crystallised from methanol in plates, m. p. 256—257° (decomp.), $[\alpha]_D$ +16·4° (*c* 0·24 in 50% aqueous EtOH) (Found: C, 60·6; H, 7·4; N, 7·5. $C_{18}H_{27}O_3N_2Cl$ requires C, 60·9; H, 7·8; N, 7·9%).

Hydrogenation of α-Deoxodihydrolycorenone with Adams Catalyst.—α-Deoxodihydrolycorenone (120 mg.) in acetic acid (10 ml.) was hydrogenated with Adams catalyst (100 mg.) for 5 hr. The product was isolated in the usual way and converted into the picrate (60 mg.), m. p. 231—232° (decomp.), identified as α-deoxodihydrolycorenine picrate by mixed m. p. and infrared spectrum.

Reduction of α-Deoxodihydrolycorenone by Lithium Aluminium Hydride.—α-Deoxodihydrolycorenone (0·3 g.) and lithium aluminium hydride (0·2 g.) in dry ether (100 ml.) were refluxed for 3 hr. After addition of moist ether and filtration of the precipitate, the ethereal solution was concentrated to 10 ml. and an excess of a saturated ethereal solution of picric acid was added. A yellow precipitate (0·3 g.) formed was collected and crystallised from methanol, to give α-*deoxodihydroepilycorenine picrate*, m. p. 215—216° (decomp.), depressed to 200—205° on admixture with α-deoxodihydrolycorenine picrate (Found: C, 53·9; H, 5·7; N, 10·3. $C_{24}H_{30}O_{10}N_4$ requires C, 53·9; H, 5·7; N, 10·5%). The infrared spectrum was not identical with that of α-deoxodihydrolycorenine picrate. The base regenerated from the picrate was an oil, $[\alpha]_D$ +16·0° (*c* 0·88).

The same compound was obtained by the reduction of α-deoxodihydrolycorenone with sodium borohydride in methanol.

Reduction of Hippeastrine by Lithium Aluminium Hydride.—Hippeastrine (0·9 g.) and lithium aluminium hydride (0·3 g.) were heated under reflux in tetrahydrofuran (20 ml.) for 5 hr. The mixture was worked up in the usual manner, and the isolated tetrahydrohippeastrine crystallised from ether as deliquescent prisms. The *tri*-p-*nitrobenzoate* was prepared with *p*-nitrobenzoyl chloride in pyridine and had m. p. 184° (decomp.) (Found: C, 58·2; H, 3·7; N, 7·2. $C_{36}H_{30}O_{14}N_4$ requires C, 58·2; H, 4·1; N, 7·6%).

Lycorine β-Methiodide from Tetrahydrohippeastrine.—Dry tetrahydrohippeastrine (0·4 g.) and toluene-*p*-sulphonyl chloride (0·275 g.) were kept in dry pyridine (10 ml.) at room temperature overnight, then heated at 80—90° for 1 hr. After evaporation under reduced pressure, the residue taken up in water (40 ml.), washed with ether and chloroform, and passed through a column of Amberlite I.R.A.-400 resin (OH-form). The column was washed with water, and the combined eluate and washings were washed 5 times with ether and then acidified with dilute hydriodic acid. After evaporation of the solution under reduced pressure, the residue was

passed in ethanol through alumina. Elution with ethanol yielded prisms (0·15 g.), m. p. 280° (decomp.) (from ethanol), $[\alpha]_D$ +136° (*c* 0·95 in H_2O), identical in mixed m. p. and infrared spectrum with authentic lycorine β-methiodide (Found: C, 46·1; H, 5·0. Calc. for $C_{17}H_{20}O_4NI,H_2O$: C, 45·7; H, 5·0%).

Epihæmanthamine Methiodide from Tazettadiol.—Dry tazettadiol (0·3 g.) was dissolved in dry pyridine (3 ml.) and freshly distilled thionyl chloride (0·15 ml.) added in portions under cooling. The mixture was kept overnight at 0°, then water was added to decompose the excess of reagent, and the whole evaporated under reduced pressure. The residue dissolved in water, was passed through a column of Amberlite I.R.A.-400 resin (OH-form). The eluate and washings were combined, washed several times with ether, neutralised with dilute hydriodic acid, and concentrated to dryness under reduced pressure. The residue was chromatographed in ethanol over alumina. Elution with ethanol yielded no crystalline substance. Elution with methanol gave prisms, m. p. 280° (decomp.), identical in m. p. and infrared spectrum with authentic epihæmanthamine methiodide (for which we thank Drs. Wildman and Fales) (Found: C, 48·4; H, 5·4; N, 3·2. Calc. for $C_{18}H_{22}O_4NI$: C, 48·8; H, 5·0; N, 3·2%).

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759. *Organosilicon Compounds. Part XXI.* Some Compounds Containing Phosphorus.*

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Organosilicon compounds containing phosphorus have been prepared, including phosphonates [*e.g.*, $PhMe_2Si{\cdot}CH_2{\cdot}P(O)(OBu^n)_2$], phosphine oxides [*e.g.*,(p-$MeC_6H_4Me_2{\cdot}Si{\cdot}CH_2)_3PO$], phosphates [*e.g.*, ($p$-$Me_3Si{\cdot}C_6H_4{\cdot}O)_3PO$], and a phosphinic acid (p-$Cl{\cdot}C_6H_4Me_2{\cdot}Si{\cdot}CH_2)_2P(O){\cdot}OH$.

Interest attaches to organosilicon compounds containing phosphorus because of the possibility of modifying the properties of Silicones (particularly lubricating power and flame-resistance) by introduction of phosphorus-containing groups. We have prepared several compounds containing silicon attached to phosphorus through carbon or carbon and oxygen. A few such compounds have been reported previously.[1-5]

Interaction of the appropriate organosilylmethyl halides with sodium salts of the type $NaP(O)(OR)_2$ has been used to give the phosphonates $Me_3Si{\cdot}CH_2{\cdot}P(O)(OR)_2$ (R = n-C_4H_9, n-C_5H_{11}), $ArMe_2Si{\cdot}CH_2{\cdot}P(O)(OBu^n)_2$ (Ar = Ph, p-Me·C_6H_4, and p-Cl·C_6H_4), and $Me_3Si{\cdot}O{\cdot}SiMe_2{\cdot}CH_2{\cdot}P(O)(OBu^n)_2$. The products are liquids, stable enough to be fractionally distilled at reduced pressure.

The solid phosphine oxides $(Me_3Si{\cdot}CH_2)_3PO$ and $(p$-$Me{\cdot}C_6H_4Me_2{\cdot}Si{\cdot}CH_2)_3PO$ have been prepared from the appropriate $\geq Si{\cdot}CH_2{\cdot}MgCl$ compound and phosphorus oxychloride in ether. The same reaction involving the Grignard reagent p-$Cl{\cdot}C_6H_4Me_2{\cdot}Si{\cdot}CH_2{\cdot}MgCl$ gave only the phosphinic acid, $(p$-$Cl{\cdot}C_6H_4Me_2{\cdot}Si{\cdot}CH_2)_2P(O){\cdot}OH$.

The phosphates $(Me_3Si{\cdot}CH_2{\cdot}O)_3PO$ (a liquid stable to distillation at reduced pressure) and (p-$Me_3Si{\cdot}C_6H_4{\cdot}O)_3PO$ (a solid) were prepared from phosphorus oxychloride and the

* Part XX, *J.*, 1957, 955.

[1] Frisch and Lyons, *J. Amer. Chem. Soc.*, 1953, **75**, 4078.

[2] Gilbert and Precopio, Abs. Papers, 125th Meeting of the American Chemical Society, 1954, p. 16N; Gilbert, U.S.P. 2,768,193/1956; *Chem. Abs.*, 1957, **51**, 5816.

[3] Keeber and Post, *J. Org. Chem.*, 1956, **21**, 509.

[4] Chernyshev and Petrov, *Doklady Akad. Nauk S.S.S.R.*, 1955, **105**, 282; *Chem. Abs.*, 1956, **50**, 11,283.

[5] Seyferth, *J. Amer. Chem. Soc.*, 1958, **80**, 1136.

sodium salts of trimethylsilylmethanol and *p*-trimethylsilylphenol in ether. Use of the latter salt with dimethylphosphorochloridate similarly gave the compound *p*-$Me_3Si{\cdot}C_6H_4{\cdot}OP{\cdot}(O)(OMe)_2$.

Tristrimethylsilylmethylphosphine oxide decomposes in nitrogen at 270°, hexamethyldisiloxane probably being a product. Di-n-butyl trimethylsilylmethylphosphonate decomposes with polymerization on boiling at atmospheric pressure.

Experimental

General.—In fractional distillations special precision-made Vigreux columns (*ca.* 15 theoretical plates) were used.

(Aryldimethylsilyl)methyl Chlorides.—These were made by boiling the appropriate ArMgBr compounds with chloro(chloromethyl)dimethylsilane in ether for 12 hr., and had the following properties: (Ar =) Ph, b. p. 134—137°/48 mm.; *p*-Me·C_6H_4, b. p. 120—122°/12 mm., 136—138°/26 mm. (previously [6] reported incorrectly as 138—140°/12 mm.); *p*-Cl·C_6H_4, b. p. 102—104°/3 mm. (previously [6] reported incorrectly as 133°/3 mm.), n_D^{20} 1·5342.

Phosphonates.—Bromomethyltrimethylsilane (1 mol.) was boiled for 12 hr. with a light petroleum (b. p. 60—80°) solution of sodium (1 mol.) in dialkyl hydrogen phosphite (1 mol.). Washing with water followed by fractionation gave di-n-butyl trimethylsilylmethylphosphonate [3] (25%), b. p. 154—158°/17 mm., or *di-n-pentyl trimethylsilylmethylphosphonate* (36%), b. p. 186—188°/18 mm., n_D^{20} 1·4418 (Found: C, 55·0; H, 11·0. $C_{14}H_{33}O_3PSi$ requires C, 54·5; H, 10·8%). Similarly from (chloromethyl)pentamethyldisiloxane, with 23 hr. of refluxing (but with filtration to remove sodium chloride instead of washing), was obtained *di-n-butyl pentamethyldisiloxanylmethylphosphonate* (23%), b. p. 150—152°/10 mm., n_D^{20} 1·4251 (Found: C, 46·9; H, 9·7. $C_{14}H_{35}O_4PSi_2$ requires C, 47·4; H, 9·9%).

Similarly from aryl(chloromethyl)dimethylsilanes were prepared di-n-butyl aryldimethylsilylmethylphosphonates as follows: (aryl =) *phenyl* (40%), b. p. 200—202°/10 mm., n_D^{20} 1·4864 (Found: C, 59·6; H, 9·5. $C_{17}H_{31}O_3PSi$ requires C, 59·6; H, 9·1%); p-*chlorophenyl* (11%), b. p. 186·5—188°/2 mm., n_D^{20} 1·4942 (Found: C, 54·5; H, 8·4. $C_{17}H_{30}O_3ClPSi$ requires C, 54·2; H, 8·0%); p-*tolyl* (32%, in this case refluxing was for 36 hr.), b. p. 187—189°/2·6 mm., n_D^{20} 1·4879 (Found: C, 60·3; H, 9·2. $C_{18}H_{33}O_3PSi$ requires C, 60·6; H, 9·3%).

Diethyl trimethylsilylmethylphosphonate,[2] b. p. 118·5—121°/22 mm., was obtained in 25% yield by refluxing together equimolecular quantities of bromomethyltrimethylsilane and triethyl phosphite until the temperature rose from 96° to 120° (5 days), and then fractionating. Diethyl pentamethyldisiloxanylmethylphosphonate [3] (41%), b. p. 154—156°/36 mm., was prepared similarly from chloromethylpentamethyldisiloxane by refluxing for 42 hr., during which the temperature of the mixture rose from 153° to 195°.

Phosphine Oxides.—Phosphorus oxychloride (14 g., 0·092 mole) in ether (50 ml.) was added slowly, with cooling to −5°, to the Grignard reagent from magnesium (6·7 g., 0·28 g.-atom) and bromomethyltrimethylsilane (4·6 g., 0·27 mole) in ether (150 ml.), and the mixture was boiled for 13 hr. After the usual hydrolysis procedure the ether layer was evaporated to dryness and the residue was recrystallised from ethanol, to give tristrimethylsilylmethylphosphine oxide (14·5 g., 51%), m. p. 182° (Found: C, 47·0; H, 10·9. Calc. for $C_{12}H_{33}OPSi_3$: C, 46·7; H, 10·8%). (This compound was recently prepared by a different route.[5])

Similarly from chloromethyldimethyl-*p*-tolylsilane and *p*-bromophenyltrimethylsilane, respectively, but with 18 hours' refluxing, were obtained *tris(dimethyl-*p*-tolylsilylmethyl)phosphine oxide*, m. p. 111·5° (from ethanol) (Found: C, 67·3; H, 8·6. $C_{30}H_{45}OPSi_3$ requires C, 67·1; H, 8·45%), and tris-(*p*-trimethylsilylphenyl)phosphine oxide, m. p. 259° (from ethanol) (cf. ref. 1). A similar procedure involving chloromethyl-*p*-chlorophenyldimethylsilane gave only *bis*-(p-*chlorophenyldimethylsilylmethyl)phosphinic acid*, m. p. 95° (from ethanol) (Found: C, 50·4; H, 5·9. $C_{18}H_{25}O_2Cl_2PSi_2$ requires C, 50·1; H, 5·85%).

An attempt to prepare tris(pentamethyldisiloxanylmethyl)phosphine oxide by this method was unsuccessful, an unidentified solid of m. p. 140° being obtained (Found: C, 29·0; H, 10·2%).

Phosphates.—Sodium (3·5 g., 0·15 g.-atom.) was dissolved in trimethylsilylmethanol (15 g., 0·15 mole) in ether (100 ml.), phosphorus oxychloride (7·7 g., 0·05 mole) in ether (50 ml.) was added, and the mixture was boiled for 16 hr. After filtration, the residue was distilled and the

[6] Eaborn and Jeffrey, *J.*, 1954, 4266.

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distillate fractionated to give *tristrimethylsilylmethyl phosphate* (3·2 g., 18%), b. p. 134—136°/5 mm., n_D^{20} 1·4331 (Found: C, 40·7; H, 9·4. $C_{12}H_{33}O_4PSi_3$ requires C, 40·4; H, 9·3%).

Similarly from *p*-trimethylsilylphenol (but without distillation of the product) was obtained *tris*-p-*trimethylsilylphenyl phosphate* (64%), m. p. 99° (from ethanol) (Found: C, 59·8; H, 7·4. $C_{27}H_{39}O_4PSi_3$ requires C, 59·7; H, 7·25%), and from *p*-trimethylsilylphenol (0·1 mole) and dimethyl phosphorochloridate (0·1 mole) was obtained *dimethyl* p-*trimethylsilylphenyl phosphate* (44%), b. p. 152—154°/4 mm., n_D^{20} 1·4862 (Found: C, 47·8; H, 6·9. $C_{11}H_{19}O_4PSi$ requires C, 48·1; H, 7·0%).

Thermal Decomposition.—When tristrimethylsilylmethylphosphine oxide was refluxed in a slow stream of nitrogen, with continuous removal of volatile material from the top of the condenser, the temperature of the boiling liquid fell from 270° to 220° during 3 hr., and a little liquid of b. p. 95—103°, n_D^{20} 1·3771, was collected. This gave silica on burning, and is believed to be hexamethyldisiloxane (b. p. 101°, n_D^{20} 1·3774).

When di-n-butyl trimethylsilylmethylphosphonate was boiled under similar conditions for 6 hr., a little liquid of b. p. 102—104°, n_D^{20} 1·387, was collected and the residue became dark brown. Some porous pot was added and the heating continued for 1 hr.; the residue was transformed into a brittle white solid insoluble in alcohol or hydrocarbons.

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THE UNIVERSITY, LEICESTER. [*Received, June 19th*, 1959.]

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760. *A New Type of Transition Metal–Cyclopentadiene Compound.**

By M. L. H. GREEN, L. PRATT, and G. WILKINSON.

The reduction of cobalticenium and rhodicenium halides by sodium borohydride or by lithium aluminium hydride forms the neutral compound in which one π-cyclopentadienyl ring has been converted into a cyclopentadiene group, π-$C_5H_5(C_5H_6)M$. The deuteride π-$C_5H_5(C_5H_5D)Co$ was obtained by reduction with lithium aluminium deuteride, and a methyl derivative, π-$Me{\cdot}C_5H_4(Me{\cdot}C_5H_5)Co$, was obtained from 1,1′-dimethylcobalticenium bromide. A monomethyl derivative, π-C_5H_5(1-*endo*-$Me{\cdot}C_5H_6$)Co, was prepared by the action of methyl iodide on cobaltocene; a trichloromethyl compound obtained previously by reaction of carbon tetrachloride with cobaltocene is shown to be similar to the 1-*endo*-methyl derivative. Reduction of the 1-*endo*-trichloromethyl compound with lithium aluminium hydride gives a 1-*endo*-dichloromethyl analogue.

Infrared and high-resolution nuclear magnetic resonance spectra of these compounds and some related olefin–transition metal complexes are described, and the structures of the molecules are discussed.

REACTION of anhydrous cobalt chloride with sodiocyclopentadiene in tetrahydrofuran produces the paramagnetic neutral di-π-cyclopentadienylcobalt(II) cobaltocene.[1] In attempts some years ago to prepare similarly the rhodium analogue from rhodium trichloride, a small yield of stable orange-yellow crystals was obtained at 150° *in vacuo*. Analysis and molecular-weight determination gave the formula $C_{10}H_{11}Rh$, and magnetic-susceptibility measurements showed the compound to be diamagnetic.

It has been shown that essentially quantitative yields of this rhodium compound can be obtained by reduction of the di-π-cyclopentadienylrhodium(III) (rhodicenium) ion in aqueous ethanol by sodium borohydride. A cobalt compound, $C_{10}H_{11}Co$, was obtained similarly and by reduction of anhydrous cobalticenium halides with lithium aluminium hydride in tetrahydrofuran or 1,2-dimethoxyethane. The latter reaction has allowed the

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[1] Wilkinson, Birmingham, and Cotton, *J. Inorg. Nuclear Chem.*, 1956, **2**, 95.

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preparation of the monodeuterium compound, $C_{10}H_{10}DCo$, by use of lithium aluminium deuteride.

On the basis of the early studies, Liehr [2] suggested that the rhodium compound was a di-π-cyclopentadienylrhodium hydride, similar in stoicheiometry to the di-π-cyclopentadienylrhenium hydride,[3] but with a different type of metal–hydrogen bond. Detailed

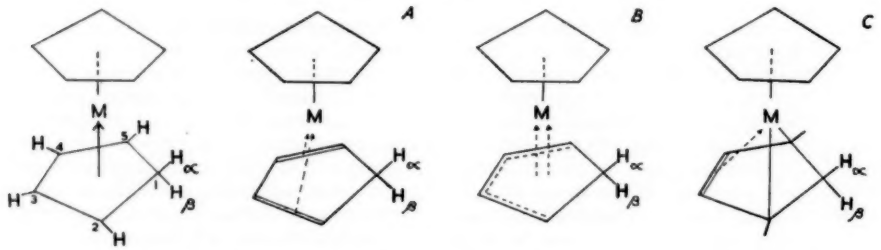
TABLE 1. *Cyclopentadiene–metal complexes.*

Compound	Form	M. p.	Ultraviolet and visible absorption (λ in mμ)
π-$C_5H_5(C_5H_6)Co$	Wine-red crystals	98—99°	397 (ε $5{\cdot}27 \times 10^3$), 327 (ε $9{\cdot}27 \times 10^3$), 263·8 (ε $1{\cdot}78 \times 10^5$)
π-$C_5H_5(C_5H_5D)Co$	,, ,,	78—79	398 (ε $4{\cdot}2 \times 10^3$), 328 (ε $8{\cdot}79 \times 10^3$), 264·7 (ε $2{\cdot}10 \times 10^5$)
π-$CH_3{\cdot}C_5H_4(Me{\cdot}C_5H_5)Co$	Dark red oil	~—5	—
π-$C_5H_5(1\text{-}endo\text{-}Me{\cdot}C_5H_5)Co$	Red oil	~—10	—
π-$C_5H_5(1\text{-}endo\text{-}CHCl_2{\cdot}C_5H_5)Co$	Orange-red crystals	50—51	—
π-$C_5H_5(1\text{-}endo\text{-}CCl_3{\cdot}C_5H_5)Co$ ...	,, ,,	79—80	400 (ε $9{\cdot}94 \times 10^3$), 331 (ε $2{\cdot}40 \times 10^4$), 272·5 (ε $1{\cdot}34 \times 10^5$)
π-$C_5H_5(C_5H_6)Rh$	Orange-yellow crystals	121—122	396 (ε $2{\cdot}84 \times 10^3$), 297 (ε $3{\cdot}01 \times 10^3$), 236·5 (ε $1{\cdot}97 \times 10^4$)

studies on a series of compounds of similar type (Table 1) now described show that this suggestion must be discarded.

The infrared and high-resolution nuclear magnetic resonance spectra discussed below indicate that in the $C_{10}H_{11}M$ compounds there is one π-cyclopentadienyl ring bound to the metal atom as in other di- and mono-π-cyclopentadienyl-metal compounds.

FIG. 1.



The electronic requirements of the metal atom in known π-cyclopentadienylcobalt and rhodium compounds, *e.g.*, π-$C_5H_5Co(CO)_2$ [4] and π-C_5H_5(cyclo-octa-1,5-diene)Rh,[5] indicate that the remaining organic part of the $C_{10}H_{11}M$ compounds, a C_5H_6 group, must furnish four bonding electrons in order that the metal atom shall achieve the formal inert-gas configuration and that the observed diamagnetism be explained. The chemical properties of the compounds, and the interpretation given below of their infrared and nuclear magnetic resonance spectra, are in agreement with a molecular configuration shown in Fig. 1. The C_5H_6 grouping contains one methylene group in which the hydrogen atoms (H_α and H_β) are not equivalent, and four ⩾C–H groups. In the substituted compounds, one hydrogen atom (H_α) is replaced by the substituent group. H_α and the groups replacing it are probably in the *endo*-configuration, *i.e.*, on the side of the C_5H_6 ring nearer to the metal atom. The hydrogen atoms on $C_{(2)}$ and $C_{(5)}$ are equivalent, but differ from the equivalent ones on $C_{(3)}$ and $C_{(4)}$. It is also probable that these four carbon atoms lie in the same plane and that the four electrons which bond the C_5H_6 group to the metal are associated with

[2] Liehr, *Naturwiss.*, 1957, **44**, 61.
[3] Green, Pratt, and Wilkinson, *J.*, 1958, 3916.
[4] Piper, Cotton, and Wilkinson, *J. Inorg. Nuclear Chem.*, 1955, **1**, 165.
[5] Chatt and Venanzi, *J.*, 1957, 4735.

these carbon atoms. The detailed bonding of this group to the metal atom is discussed after the evidence for the molecular configuration has been presented.

Chemical Properties.—The π-cyclopentadienyl(cyclopentadiene)Co(or Rh) compounds could not be prepared by electrolysis of neutral or alkaline aqueous solutions of the $(\pi$-$C_5H_5)_2M^+$ ions, or by reduction of such solutions by sodium amalgam, sodium dithionite, or Devarda's alloy. The reduction solely by complex hydrides suggests that hydride-ion attack, either on the π-C_5H_5 ring or through initial attack on the metal atom, is involved. Since borohydride and aluminium hydride do not usually cleave carbon–carbon bonds, no opening of the five-membered ring is to be expected. Thus we can write $(\pi$-$C_5H_5)_2M^+ + H^-$(or D^-) = $(\pi$-$C_5H_5)MC_5H_5H$(or D).

The presence of the intact five-membered ring is also indicated by the reaction of the compounds with acids. With 2N-hydrochloric acid, $C_{10}H_{11}Rh$ gives about a 50% yield of the $(\pi$-$C_5H_5)_2Rh^+$ ion, which was characterised by precipitation reactions and by its absorption spectrum.[6] A gas is also evolved which has been found to consist of hydrogen (~50%) together with C_5 olefinic hydrocarbons (mass 68, probably mainly cyclopentene) and a trace of butenes; some insoluble matter containing metal is also produced, presumably associated with the degradation leading to olefins. This reaction has a parallel in the reaction of the compounds with carbon tetrachloride at room temperature to form chloroform and the respective $(\pi$-$C_5H_5)_2M^+$ chlorides as the main products, together with insoluble tar and some unidentified solvent-soluble olefins. From the products formed by air-oxidation of $C_{10}H_{11}Co$, considerable amounts of the cobalticenium ion can be recovered on extraction with water or dilute acid.

The simple hydrogen-transfer reactions, *e.g.*:

$$\pi\text{-}C_5H_5CoC_5H_6 + H^+_{aq.} = (\pi\text{-}C_5H_5)_2Co^+_{aq.} + H_2$$

$$\pi\text{-}C_5H_5CoC_5H_6 + CCl_4 = (\pi\text{-}C_5H_5)_2Co^+Cl^- + CHCl_3$$

suggest the presence in the molecules of a hydridic hydrogen atom.

The compounds are unaffected by hydrogenation in presence of Adams catalyst, and a Kuhn–Roth analysis for a *C*-Me group was negative. No reaction was observed with nitric oxide at room temperature and atmospheric pressure, and no hydrogen-transfer was obtained with acridine, the rhodium compound being recovered after three days. *N*-Bromosuccinimide in benzene with $C_{10}H_{11}Co$ gave cobalticenium bromide quantitatively, whilst benzaldehyde in alkaline solution gave the cobalticenium ion together with benzyl alcohol and benzoic acid.

The chemical properties thus show the presence of a cyclic C_5H_6 unit but indicate that the $-CH_2-$ group has unusual chemical behaviour, one of the hydrogen atoms being readily lost. In fact, the derivatives of the $C_{10}H_{11}Co$ compound have been prepared, where the substituent group, replacing H_α, is 1-*endo*.

π-Cyclopentadienyl-(1-*endo*-methylcyclopentadiene)cobalt was prepared by a different route from that used for the $C_{10}H_{11}M$ compounds. It was known [1] that cobaltocene reacts with organic halides to give cobalticenium salts and unidentified hydrocarbon-soluble red cobalt compounds without evolution of gas. It seemed reasonable to assume that with methyl iodide a methyl-substituted derivative similar to the $C_{10}H_{11}M$ compounds was formed, and this has proved to be the case, the reaction being:

$$2(\pi\text{-}C_5H_5)_2Co + CH_3I = (\pi\text{-}C_5H_5)_2CoI + \pi\text{-}C_5H_5(1\text{-}Me\text{-}C_5H_5)Co$$

The spectra of this methyl derivative, which are discussed below, show that it contains a $-CHMe-$ group.

The 1-endo-*Chloromethyl Derivatives.*—Other workers [7] have recently reported a reaction between cobaltocene and carbon tetrachloride. We similarly obtained the orange-red crystalline product $C_{10}H_{10}(CCl_3)Co$. The infrared and nuclear magnetic resonance

[6] Cotton, Whipple, and Wilkinson, *J. Amer. Chem. Soc.*, 1953, **75**, 3586.
[7] Katz, Weiher, and Voigt, *ibid.*, 1959, **80**, 6459.

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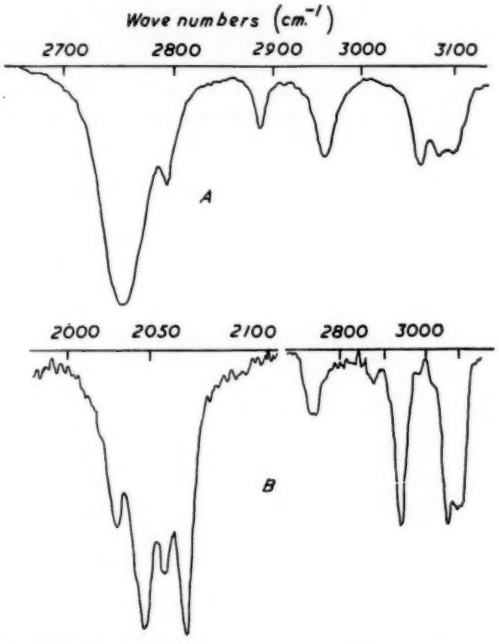
spectra of this compound closely resemble those of the 1-*endo*-methyl derivative (Tables 2 and 3 and Fig. 3) and it must have a similar structure, with a $-CH(CCl_3)-$ group. In an attempt to reduce the 1-*endo*-trichloro-derivative with lithium aluminium hydride to the methyl analogue, the main product formed was the 1-*endo*-dichloromethyl compound, π-C_5H_5(1-$CHCl_2$·C_5H_5)Co. Its properties agree with formulation as the $-CH(CHCl_2)-$ derivative.

Another compound, π-methylcyclopentadienyl(methylcyclopentadiene)cobalt, was obtained by reduction of 1,1′-dimethylcobalticenium chloride with sodium borohydride. It

FIG. 2. *Infrared spectra of* π-$C_5H_5(C_5H_6)Co$ (*A*) *and* π-$C_5H_5(C_5H_5D)Co$ (*B*) *in the* 2600—3200 *cm.*$^{-1}$ *region* (LiF *optics*).



is a very reactive, thermally unstable liquid. Although isomers might have been expected from the method of formation, chromatography showed no evidence for them. This derivative develops hydrogen pressure in a sealed tube and eventually solidifies to form dark red-black crystals, m. p. ~33°; the reaction may be written thus:

$$\pi\text{-Me·}C_5H_4(\text{Me·}C_5H_5)Co \longrightarrow (\pi\text{-Me·}C_5H_4)_2Co + \tfrac{1}{2}H_2$$

Infrared Spectra.—The spectra to 650 cm.$^{-1}$ are given in the Experimental section. High-resolution spectra in the region 2700—3300 cm.$^{-1}$ are given in Table 2 and Fig. 2. In the spectra of all the compounds there are bands characteristic of a π-C_5H_5–metal grouping (cf. ref. 8), including a single sharp C–H stretching band at 3100 cm.$^{-1}$. Both of the $C_{10}H_{11}M$ compounds show two bands in the region where aliphatic C–H stretching frequencies normally occur, at 2948 and 2882 cm.$^{-1}$ for the rhodium compound and 2942 and 2871 cm.$^{-1}$ for the cobalt compound. These bands have the appearance of those due to a methylene group.[9] In the deuterium compound π-$C_5H_5(C_5H_5D)Co$, however, the

[8] Piper and Wilkinson, *J. Inorg. Nuclear Chem.*, 1956, **3**, 104.
[9] Bellamy, "The Infra-red Spectra of Complex Molecules," 2nd edn., Methuen and Co., London, 1958.

2871 cm.$^{-1}$ band disappears and *does not* reappear in the expected region (2871/$\sqrt{2}$ cm.$^{-1}$); therefore it cannot be assigned as a fundamental C–H stretching frequency. In agreement with this, no band is observed near 2870 cm.$^{-1}$ in the trichloromethyl derivative. Similarly the peak at about 2780 cm.$^{-1}$ in the $C_{10}H_{11}M$ compounds is not found in the 1-*endo*-methyl or 1-*endo*-chloromethyl derivative or in similar arene–iron compounds, *e.g.*, $C_6H_6(C_5H_6)Fe$ (to be described in a later paper). It therefore seems reasonable to ascribe this band as an overtone or combination in the C_5H_6–metal system. The band at 2942 cm.$^{-1}$ remains in the same position in the deuterated compound but with a slightly increased intensity; this band could therefore be assigned as a C–H fundamental from the C_5H_6 group.

The bands at approximately 3050 and 3080 cm.$^{-1}$ which are found in the spectra of all the compounds are in the region of olefinic C–H stretching modes.

A most unusual feature of the $C_{10}H_{11}M$ compounds is a band at about 2750 cm.$^{-1}$, which is one of the strongest in their spectra. It may be noted that very few fundamental

TABLE 2. *Infrared spectra in* 2700—3200 *cm.*$^{-1}$ *region* (*cm.*$^{-1}$).

π-$C_5H_5(C_5H_6)Rh$	π-$C_5H_5(C_5H_6)Co$	π-$C_5H_5(C_5H_5D)Co$ [a]	π-$C_5H_5(C_5H_5CH_3)Co$	π-$C_5H_5(C_5H_5CCl_3)Co$	Assignment [b]
3100m	3096m	3105m	3100m	3100m	1
3080m	3076m	3068m	3088m	3085m	2
—	—	—	3075m	—	2
3056m	3053m	3042m	3045m	3066m	2
—	—	—	2960s	—	3
—	—	—	2850m	—	3
—	—	—	—	2956w	4
2948m	2942m	2932m	2912s	2924m	5
2882w	2871w	—	—	—	4
2784w	2780w	—	—	—	4
2758s	2742s	2745w	—	—	6
—	—	2076s	—	—	7
—	—	2057s	—	—	7
—	—	2039s	—	—	7
—	—	2017s	—	—	7

[a] Isotopic purity ~95%. [b] 1, C–H stretch of π-C_5H_5; 2, CH:CH stretch; 3, –Me stretch of CH_3; 4, probably overtone or combination band; 5, C–Hβ stretch; 6, C–Hα stretch; 7, C–D stretch.

stretching frequencies in the region ~2750 cm.$^{-1}$ have been reported (cf. ref. 9), the most notable being that of the aldehyde group. Since this band at ~2750 shifts by approximately the expected value [ν_H(obs.)/ν_D(obs.) = 1·34] in π-$C_5H_5(C_5H_5D)Co$, it must be assigned as a fundamental C–H stretching frequency. The marked splitting of the C–D peaks, which is not observed for the corresponding C–H peak even under the highest resolution, may be attributed to coupling with other vibrational frequencies.

In the formation of the deuterated derivative by reduction of the cobalticenium ion with lithium aluminium deuteride, it is probable that a –CHD– group is formed. Since the strong C–H peak is also absent in the monosubstituted cobalt derivatives, it may be assigned to the methylene proton which is replaced in these compounds and in the deutero-compound.

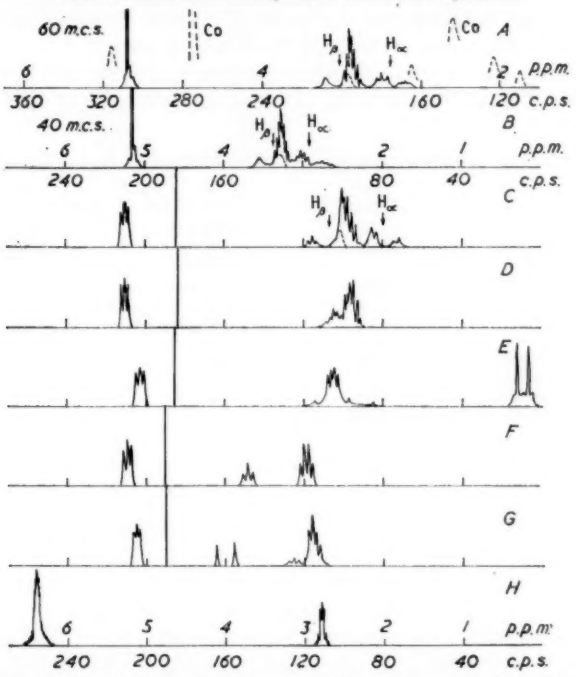
The other fundamental aliphatic C–H stretching frequency at 2948 cm.$^{-1}$ (Rh) and 2942 cm.$^{-1}$ (Co) which occurs at about the same place in all the compounds is assigned to the C–H stretching frequency of the other methylene proton. The marked difference in the two methylene C–H bands is confirmed by the nuclear magnetic resonance spectra. It seems likely that the unusually low and intense stretching frequency of the reactive methylene-hydrogen atom may be caused by the close approach of one of the protons, H_α, to the metal atoms causing steric or electrostatic interactions. Therefore we assign the bands at 2758 (Rh) and 2742 (Co) to the C–Hα stretching frequency and those at 2948 (Rh) and 2942 (Co) to the C–Hβ stretching frequency (Fig. 2).

The 1-*endo*-methyl derivative shows that in addition to the C–Hβ stretch at 2912 cm.$^{-1}$ there are two more strong bands in the aliphatic C–H stretching region, at 2960 and

2850 cm.$^{-1}$. These are assigned to the asymmetrical and symmetrical C–H stretching frequencies of the methyl group. Similarly in the 1-*endo*-dichloromethyl derivative there is a band at 2962 cm.$^{-1}$ which may be attributed to the C–H stretching frequency of the $CHCl_2$ group.

High-resolution Nuclear Magnetic Resonance Spectra.—The spectra were obtained at 40 and 60 Mc./sec. (Table 3) and are shown in Fig. 3. The sharpness of the lines in all the

FIG. 3. *High-resolution proton magnetic resonance spectra of cyclopentadiene compounds of rhodium and cobalt, relative to tetramethylsilane as internal reference.*



A, π-$(C_5H_5)(C_5H_6)Rh$ at 60 Mc./sec.; broken lines show line positions of π-$(C_5H_6)(C_5H_6)Co$ at 60 Mc./sec (All other spectra at 40 Mc./sec.)
B, π-$(C_5H_5)(C_5H_6)Rh$ } Broken line indicates "hidden component" of Hβ doublet. Arrows indicate ap-
C, π-$(C_5H_5)(C_5H_6)Co$ } proximate chemical shift positions for Hα and Hβ.
D, π-$(C_5H_5)(C_5H_5D)Co$. *E*, π-(C_5H_5)(1-*endo*-Me·C_5H_5)Co. *F*, π-(C_5H_5)(1-*endo*-CCl_2·C_5H_5)Co.
G, π-(C_5H_5)(1-*endo*-$CHCl_2$·C_5H_5)Co. *H*, Cyclopentadiene.

spectra shows that the pure compounds are diamagnetic (the broadened lines in the spectrum at 60 Mc./sec. of the $C_{10}H_{11}Co$ compound indicate that this particular sample contained some paramagnetic impurity).

In no case was a line observed in the region (7·5—17·5 p.p.m. on the high-field side of tetramethylsilane) where lines due to hydrogen atoms directly bound to a transition metal occur.[3]

All the spectra can be satisfactorily interpreted on the basis of the molecular structure of Fig. 1 for the $C_{10}H_{11}M$ compounds. They all show a strong, sharp line which is assigned to the five equivalent protons of the π-C_5H_5 group as in other metal–cyclopentadienyl compounds.[3,4] This line is single in the cobalt compounds, but in the rhodium compound it is a doublet with a separation $1·0 \pm 0·2$ cycles/sec. at both 40 and 60 Mc./sec. This splitting arises from the field-independent spin coupling interaction between the C_5H_5

TABLE 3. *Nuclear magnetic resonance data (see Fig. 3).*

Compound	Frequency (10^6 c.p.s.)	Band position (p.p.m. rel. to $SiMe_4$)	Relative intensity	Structure: Multiplicity	Structure: Sepn. bet. components (c.p.s.)	Assignment
$Rh(C_5H_5)(C_5H_8)$	40	5·13	7{5	2 (doublet)	1·0 ± 0·2	(C_5H_5) group
		~5·09	7{2	3 or 4	1—2	$H_{(3)} + H_{(4)}$
		3·54	~¼	1	—	Part of doublet of Hβ; splitting 11·2 c.p.s.; chemical shift posn. ~3·34 p.p.m.
		3·26	~2¼	⩾7	~1·1 ± 0·3	Remainder ($I = \frac{1}{2}$) of Hβ doublet + ($H_{(2)} + H_{(5)}$ at 3·25 p.p.m.
		3·02	1{~¾	~5	~2·2 }	H_α doublet; sepn. 11·2 c.p.s.
		2·74	1{~¼	~4	~2 }	chemical shift posn. ~2·92 p.p.m.
$Rh(C_5H_5)(C_5H_8)$	60	5·14	7{5	2 (doublet)	1·0 ± 0·2	(C_5H_5) group
		~5·09	7{2	3 or 4	1—2	$H_{(3)} + H_{(4)}$
		3·46	~¼	1 (~6 broad)	—	Part of Hβ doublet; splitting 11·2 c.p.s.; chemical shift posn. ~3·34 p.p.m.
		~3·26	~2¼	⩾7	~1·1 ± 0·3	Remainder of Hβ doublet ($I = \frac{1}{2}$) + ($H_{(2)} + H_{(5)}$) at 3·25 p.p.m.
		~2·99	1{~¾	3 to 5	~2 }	H_α doublet; splitting 11·2 c.p.s
		2·80	1{~¼	3 or 4	~2 }	chemical shift posn. ~2·9 p.p.m.
$Co(C_5H_5)(C_5H_8)$	40	5·20	2	3 (triplet)	1·9 ± 0·2	$H_{(3)} + H_{(4)}$
		4·59	5	1		(C_5H_5) group
		2·87	~¼	3 (triplet)	2·2 ± 0·3	Part of Hβ doublet; splitting 12·7 c.p.s.; chemical shift posn. at ~2·68 p.p.m.
		2·45	~2¼	5 to 6	{ — { 2·0 ± 0·3	Remainder of Hβ doublet ($I = \frac{1}{2}$) + ($H_{(2)} + H_{(5)}$); $I = 2$; possibly a quintuplet; centred at 2·43 p.p.m.
		2·08	1{~¾	2	~2·1 ± 0·3 }	Doublet of H_α; splitting = 12·7
		1·81	1{~¼	2	~2·1 ± 0·3 }	c.p.s.; chemical shift posn. at ~2·01 p.p.m.
$Co(C_5H_5)(C_5H_8)$	60	5·25	2	1 (broad)	—	$H_{(3)} + H_{(4)}$
		4·6	5	1 (broad)		(C_5H_5) group
		2·75	~¼	1 (broad)		Part of Hβ doublet; splitting 12·7 c.p.s.; chem. shift posn. at ~2·6 p.p.m.
		2·4	~2¼	1 (broad)		Remainder ($I = \frac{1}{2}$) of Hβ doublet + ($H_{(2)} + H_{(5)}$); at ~2·4 p.p.m.
		2·04	~¾	1 (broad)	}	H_α doublet; splitting 12·7 c.p.s.
		1·82	~¼	1 (broad)	}	chemical shift posn. at 1·95 p.p.m.
$Co(C_5H_5)(C_5H_8D)$	40	5·20	2	Triplet	2·0 ± 0·2	$H_{(3)} + H_{(4)}$
		4·58	5	Singlet		(C_5H_5) group
		2·64	1	Complex, pentuplet	2·1 ± 0·3	Hβ
		2·40	2	Complex, quartet	~2	$H_{(2)} + H_{(5)}$
$Co(C_5H_5)(C_5H_8Me)$ ...	40	5·07	2	Triplet	2·0 ± 0·2	$H_{(3)} + H_{(4)}$
		4·61	5	Singlet	—	(C_5H_5) group
		~2·63	3	Quartet main + others	~2 in quartet	Hβ + ($H_{(2)} + H_{(5)}$)
		0·23	3	Doublet + others	~5·8 ± 0·2	Me
$Co(C_5H_5)(C_5H_8{\cdot}CCl_3)$	40	5·23	2	Triplet	2·0 ± 0·2	$H_{(3)} + H_{(4)}$
		4·75	5	Singlet	—	(C_5H_5) group
		3·70	1	Triplet	2·5 ± 0·2	Hβ
		2·96	2	Quadruplet	bet. inner two peaks 2·0 ± 0·2 bet. outer pairs, 2·2	$H_{(2)} + H_{(5)}$
$Co(C_5H_5)(C_5H_8{\cdot}CH_2Cl_2)$	40	5·12	2	Triplet	2·0 ± 0·3	$H_{(3)} + H_{(4)}$
		4·75	5	Singlet		(C_5H_5) group
		4·12 } 3·89 }	~1	Doublet	8·9	H of $CHCl_2$ group
		3·14	~¼	Triplet	2·3 ± 0·3	Part of Hβ "doublet"
		2·89	~2¼	Complex, quadruplet	~2	Remainder of Hβ; $H_{(2)} + H_{(5)}$
C_5H_8	40	6·38	4	Complex, multiplet	<1	$H_{(2, 3, 4, 5)}$
		2·79	2	Complex, pentuplet	~1·2	$H_{(1)}$ and $H_{(2)}$ (on $C_{(1)}$)

protons and the ^{103}Rh nucleus (100% abundance, spin $\frac{1}{2}$; each proton line of the π-C_5H_5 ring is split into $2 \times \frac{1}{2} + 1 = 2$ components). Similarly the $(\pi\text{-}C_5H_5)_2Rh^+$ ion in water shows a spectrum which is a sharp doublet with a separation of about 1·0 cycle/sec. The absence of splitting in the cobalt compounds is due to rapid relaxation of the ^{59}Co nucleus which has a quadrupole moment.[10] All the cobalt compounds show a band (at about 5·2 p.p.m. relative to $SiMe_4$) on the low-field side of the C_5H_5 line. This band has three main components and has an intensity (area) corresponding to two protons relative to the C_5H_5 lines whose intensity is taken as 5. This band cannot be observed separately for the rhodium compound, although there are some incompletely resolved lines at the base of the C_5H_5 doublet. Comparisons of the total intensity of the composite band, both with that of the other bands in the spectrum and with the intensity of the cyclopentadienyl line from ferrocene in an equimolar solution, indicate that there is a band of intensity 2 analogous to those in the cobalt compounds, which is largely obscured by the C_5H_5 doublet. This band is assigned to the two *equivalent* protons on $C_{(3)}$ and $C_{(4)}$. The resonance of each of these protons is split into a doublet by the nearest proton on $C_{(2)}$ (or $C_{(5)}$) and again into a doublet by the more distant proton of $C_{(5)}$ (or $C_{(2)}$). The two separate splittings are both roughly 2 cycles/sec., and the two middle lines of the doublets overlap, under the resolution obtained, to give the observed triplet structure with a total splitting of about 4 cycles/sec. The assignment of this band to resonances of the protons remote from the CH_2 group is supported by the absence of additional splitting.

Another common feature of the spectra is the presence on the high-field side of the C_5H_5 line of a band of intensity 2, with more fine structure than the one just described. This is assigned to two equivalent protons on $C_{(2)}$ and $C_{(5)}$. A simple interpretation of its structure can be given for the trichloromethyl-cobalt derivative, where complications due to the close proximity of other resonances are absent. The resonance of each proton is split into a doublet three times over, once by the nearest proton on $C_{(3)}$ (or $C_{(4)}$) (~2 cycles/sec.), again by the more distant proton on $C_{(4)}$ (or $C_{(3)}$) (~2 cycles/sec.) and, in addition, by the single proton H_β on $C_{(1)}$ (2·5 cycles/sec.). Within the resolution obtained, the inner components of the three doublets overlap to give the observed quartet. In agreement with this interpretation, the overall splitting (6·4 cycles/sec.) is, within the limits of experimental error, equal to the sum (6·5 cycles/sec.) of the three splittings contained in the lines from the three protons producing it. A similar group of lines appears in the spectra of the other compounds, although the simple quartet structure is made more complicated by additional factors. First, the H_β resonance lies closer to this group, so that the chemical shift between them is either not much greater than the splittings or is so small that the H_β line is obscured. In either case a simple interpretation of the splittings does not account for all the lines. Secondly, in the $C_{10}H_{11}M$ compounds there is also a splitting from the additional proton (H_α) and for the rhodium compound some further splitting by the ^{103}Rh nucleus may be present.

The remaining group in the spectrum of the trichloromethyl compound has unit intensity and is assigned to the H_β proton. The splitting into a 1 : 2 : 1 triplet, with a separation between components of 2·5 cycles/sec., is attributed to spin coupling with the two equivalent protons on $C_{(2)}$ and $C_{(5)}$. The chemical shift to markedly lower fields, compared with that for the other compounds, is probably due to an inductive effect of the electronegative chlorine atoms. In the other compounds, the lines from this proton are partly or completely obscured.

The spectra of the $C_{10}H_{11}M$ compounds show two complex lines at slightly higher fields than the strong band which, on the above assignment, contains the C_5H and C_2H resonances. These weaker lines, whose combined intensity is unity, are missing in the deutero-cobalt derivative, and hence they represent the contribution from the H_α proton. Also, the replacement of H_α by a deuterium atom changes the position and structure of the

[10] Pople, *Mol. Phys.*, 1958, **1**, 168.

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visible components of the H_β resonance which occur on the low-field side of the strong band.

These changes, and the doublet structure of the H_α resonance, can be interpreted as follows. The H_α and H_β protons are in different environments, and each splits the other into a doublet. However, the chemical shift between these protons (27 cycles/sec. for $C_{10}H_{11}Co$ and 17·5 cycles/sec. for $C_{10}H_{11}Rh$ at 40 Mc./sec.) is of the same order of magnitude as the spin–spin coupling between then (12·7 and 11·2 cycles/sec., respectively). In a group of this type (H_AH_B) it is known [11] that the spectrum appears as a symmetrical quartet with the outer peaks less intense than the inner ones. The inner peak of the H_β doublet lies under the strong band and only its outer component is observed. In the $C_{10}H_{10}DCo$ derivative, the H_β proton no longer experiences the relatively large splitting by H_α, and its resonance is centred at a position which should correspond with that calculated from the lines assigned to the quadruplet in the $C_{10}H_{11}Co$ compound. The small arrows indicate the calculated positions of the unsplit resonances for H_α and H_β in the $C_{10}H_{11}M$ compounds. The calculated position of the H_β resonance in the cobalt compound does in fact agree with that observed in the deutero-derivative.

The above interpretation and calculations were assisted by measurements of the spectra at 60 Mc./sec., since chemical shifts (in cycles/sec.) are directly proportional to field strength, and spin–spin couplings are field-independent. As expected for an H_AH_B group, the splitting of each doublet is the same as at 40 Mc./sec., whilst the chemical shift separation between the doublets increases in the expected manner.

Part of the additional structure on the main components of the H_α and the H_β resonance arises from smaller splittings produced by coupling with the protons on $C_{(2)}$ and $C_{(5)}$.

In the spectrum of the $CHCl_2$ derivative the doublet (intensity equivalent to 1 proton) at 4·05 p.p.m. is assigned to the single proton of the $CHCl_2$ group. The resonance of this proton is shifted to lower fields by the adjacent chlorine atoms, and split into a doublet by H_β. Conversely, the resonance of H_β should be a doublet of the same separation (9 cycles/sec.). This doublet appears to be centred at ~3·1 p.p.m., with one component obscured by the group of lines from ($H_{(2)}$,$H_{(5)}$). The observed component shows a triplet structure, probably due to coupling with the protons on $C_{(2)}$ and $C_{(5)}$.

In the 1-*endo*-methyl derivative the resonance of the methyl protons, which occurs at a comparatively high field (0·23 p.p.m.), is more shielded than the resonances in normal aliphatic methyl groups, which may be due to the metal atom. The main doublet structure of this resonance (separation 6·8 cycles/sec.) is probably caused by coupling with the H_β proton; the additional structure may be the result of restricted rotation of the group about the C–C axis. The resonance of H_β should conversely be split by the three methyl protons into a quadruplet with the same separation between the components. This group cannot be observed, but must lie under the lines of ($H_{(2)}$,$H_{(5)}$). Intensity measurements are consistent with this interpretation.

π-Methylcyclopentadienyl(methylcyclopentadiene)cobalt.—The infrared spectrum of this compound is similar to those of the $C_{10}H_{11}M$ compounds, showing again a strong band at ~2750 cm.$^{-1}$, and therefore a $-CH_2-$ group must be present in the ($Me{\cdot}C_5H_5$) ring. This is to be expected since a hydride ion attack on the 1,1′-dimethylcobalticenium ion would probably occur at carbon atoms remote from the methyl group. The nuclear magnetic resonance spectrum shows a complicated pattern of lines, which are broadened by the presence of paramagnetic impurities. The spectrum was not analysed although the general features are consistent with the compound having the same basic molecular structure.

Butadiene-iron Carbonyl Compounds.—It is probable that the structures of the cyclopentadiene compounds discussed above are related to that of butadiene-iron carbonyl, $C_4H_6{\cdot}Fe(CO)_3$,[12] in which the C_4H_6 group supplies four electrons to the iron atom. This

[11] Pople, Schneider, and Bernstein, *Canad. J. Chem.*, 1957, **35**, 1060.
[12] Hallam and Pauson, *J.*, 1958, 642.

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group would correspond to the $C_{(2)}C_{(3)}C_{(4)}C_{(5)}$ group in the cyclopentadiene compounds. The infrared spectrum of the butadiene compound shows a main strong peak at 3050 cm.$^{-1}$ (assigned to the olefinic C–H stretching frequencies) and a weak peak at 2925 cm.$^{-1}$ (probably an overtone or combination band).

The nuclear magnetic resonance spectrum of the butadiene compound shows three symmetrical complex bands, each of an intensity corresponding to two protons. Comparison of the spectra at 40 and 60 Mc./sec. shows that the separations between the bands are chemical shifts. The low-field band at 5·28 p.p.m. is assigned to the two equivalent protons on the central carbon atoms. The bands in the high-field region are assigned to the four protons on the terminal carbon atoms. The symmetry of all the band patterns indicates that the terminal $=CH_2$ groups are equivalent, but that the two protons of this group are not equivalent. The spectrum of the 1,2,3,4-tetraphenyl derivative supports this assignment, since it shows a doublet band (separation 10 cycles/sec., intensity ~20) at low fields (6·92 + 7·16 p.p.m.) assigned to the protons on the phenyl groups, and an unresolved band (width ~3 cycles/sec., intensity ~2) at higher fields (2·38 p.p.m.), which is assigned to the two protons on the terminal carbons.

Discussion

It has been seen that the evidence given above suggests the molecular configuration shown in Fig. 1. The bonding in that part of the molecule consisting of $C_{(3)}$,$C_{(3)}$,$C_{(4)}$,$C_{(5)}$, and the metal atom can be represented in several ways, and three extreme formal structures may be considered. These are structure A, in which each double bond of a cyclopentadiene molecule independently donates two electrons to the metal; a structure B with delocalisation of these electrons; and structure C, which would result from a Diels–Alder type addition of the conjugated system of a cyclopentadiene molecule to the metal atom, with a donation of two electrons from the remaining double bond.

Similar structures can be considered for the butadiene-iron carbonyl compound for which a structure of the type B has been proposed.

It does not seem possible to arrive at a definite conclusion about the bonding in these compounds from the data at present available.

The infrared data are less consistent with structures of type C. For the $C_{10}H_{11}M$ compounds, apart from the bands which have been assigned to C–H stretching frequencies of the 1-CH_2 group, there are no strong bands in the region associated with aliphatic (sp^3) CH groups, which would be present at $C_{(2)}$ and $C_{(5)}$. For the butadiene compound also a strong band with a doublet structure would be expected for aliphatic-type methylene groups at $C_{(2)}$ and $C_{(5)}$, but this is not observed. The infrared data indicate the presence of hydrogen atoms bonded to sp^2-hybridised carbon atoms, but can be interpreted equally well by structure A or B.

These interpretations assume that the normal infrared correlation rules for C–H bonds in simple organic molecules are still valid for C–H bonds in groups which are bonded to a metal atom in organometallic compounds. This assumption is probably correct since the vibration frequency of a C–H bond depends mainly on the carbon-atom hybridisation; provided that the hybridisation is essentially sp^2, the C–H stretching frequency will not be greatly altered by variations in π-electron density at the carbon atom.

For simple organic molecules, similar correlations are found experimentally between the chemical environment of a hydrogen atom and the relative position of its nuclear (*i.e.*, proton) resonance line. If the present data are interpreted with these correlations, they agree better with structures of the type C, with only the protons on $C_{(3)}$ and $C_{(4)}$ in the lower field region associated with normal olefinic protons.

However, the correlation rules for simple organic molecules may not be valid as a criterion of bond type in organometallic compounds. The relative position of a proton resonance at a constant applied frequency depends on the extent to which it is shielded

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from the field by the local magnetic fields produced by the induced motions of the electrons around it. In an olefin group there appears to be a paramagnetic contribution to the proton-shielding from the π-electrons (ref. 13), and if the π-electrons are involved in bonding to a metal atom this contribution could be altered so as to make the resonances of

TABLE 4. *Nuclear magnetic resonance data at 40 Mc./sec.*

Compound	Band posn. (p.p.m. rel. to $Si(CH_3)_4$	Rel. int.	Structure; splitting (c.p.s.)	Assignment
Butadiene (liquid)	~6·2	2	Complex quadruplet	Centre =CH–, $C_{(2)}$, $C_{(3)}$
	~5·11	4	Complex triplet	End $=CH_2$ $C_{(1)}$, $C_{(4)}$
Butadiene-iron tricarbonyl [12]	5·28	2	Symmetrical complex triplet; 6·9	$C_{(2)}$ $C_{(3)}$ protons
	1·68	2	Double: 4·1; 2·5	$C_{(1)}$ and $C_{(4)}$ protons
	0·22	2	Double doublet: 4·1; 2·1	$C_{(1)}$ and $C_{(4)}$ protons
1,2,3,4-Tetraphenylbutadiene-iron tricarbonyl	7·16 6·92	20	Doublet (~10)	Phenyl protons
	2·38	2	Singlet (width 3)	$C_{(1)}$ and $C_{(4)}$ protons
Norbornadiene	6·62	4	Triplet	Olefin protons
	3·50	2	Septuplet	Tertiary protons
	1·95	2	Triplet	Bridging CH_2 group
Norbornadiene-iron tricarbonyl [a]	3·12	~6	Complex, doublet + unresolved line	" Olefin " and tertiary protons
	1·25	2	Triplet	Bridging CH_2 group
Norbornadiene-rhodium chloride dimer [b]	3·88	~6	Weak doublet	" Olefin " and tertiary protons
	1·20	~2	Weak singlet, unresolved	Bridging CH_2 group
Cyclo-octa-1,5-diene	5·5	4	Unresolved, singlet	Olefin protons
	2·25	8	Quadruplet	Aliphatic CH_2 protons
Cyclo-octa-1,5-diene-rhodium dimer [c]	4·25	~4	Unresolved singlet	" Olefin " protons
	2·17	~8	Broad quadruplet	? Aliphatic protons
Cyclopentadiene	6·38	4	Complex multiplet	Protons on C at posns. 2—5
	2·79	2	Complex pentuplet	Protons of CH_2 group
$(C_5H_5)(C_5H_4)Re(CO_2)$ [11]	~6·9	1	Complex band	Protons on non-bonded double bond
	~5·9	1	Complex band	
	~5·6	5	Singlet	C_5H_5 protons
	~4·7	1	Doublet (~7)	Protons of olefin group bonded to metal
	~4·3	1	Complex band	
	~3·3	2	Complex	Protons of CH_2 group
$(C_5H_5)(C_5H_6)Re(CO)_2$ [11]	~6·1	5	Singlet	C_5H_5 protons
	~4·05	2	Single band	Protons of bonded olefin group
	~2·7	4	Complex	Protons of 3-CH_2 and 5-CH_2
	~1·2	2	Complex	Protons of 4-CH_2

[a] Burton, Green, Abel, and Wilkinson, *Chem. and Ind.*, 1958, 1592. [b] Abel, Bennett, and Wilkinson, unpublished work. [c] Chatt and Venanzi, *J.*, 1957, 4735.

protons on sp^2-hybridised carbon atoms appear at higher fields than in simple olefins. In several compounds which contain non-conjugated olefin molecules bonded to metal atoms, we have observed (Table 4) that the resonance lines of protons in the " olefin " groups do not always appear in the olefin region, as has already been reported in the compounds π-cyclopentadienyl(cyclopentadiene)rhenium dicarbonyl and its reduced derivative.[14] In metal derivatives of conjugated olefins, such as those of cycloheptatriene and those discussed in the present paper, only some of the normal olefinic proton resonances of the parent olefin are shifted to higher fields, which may indicate that the π-electrons are localised between certain carbon atoms and not as much delocalised as was suggested previously.[15] However, the shifts cannot be interpreted solely in terms of π-electrons, since it is probable that there is an additional contribution to the shielding from

[13] Jackman, personal communication.
[14] Green and Wilkinson, *J.*, 1958, 4314.
[15] Abel, Bennett, Burton, and Wilkinson, *J.*, 1958, 4559.

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the electrons of the metal atom, and as yet there are insufficient data for organometallic compounds of known structure to allow definite conclusions concerning the bonding to be made. Hence in either of the two types of compound the infrared and nuclear magnetic resonance data suggest different structures, but they can be reconciled on the basis of structure A or B rather than C because it is felt that at present infrared must be preferred to nuclear magnetic resonance data as a criterion of bond type.

The extent to which the diene of structure A is delocalised (as in B) is not determined by the spectroscopic evidence. Since the bond order of the 2,3-bond in butadiene and probably also that of the 3,4-bond in cyclopentadiene is essentially that of a single bond, the bonding in structure A can be roughly pictured in the manner described [16] for the bonding between unconjugated olefins and metal atoms, in which it is believed that there is a feedback of electrons from filled *d*-orbitals of the metal to the anti-bonding orbitals on the carbon atoms of the double bond. For the conjugated olefins an additional bonding could result from a further overlap between the resultant (d–p_π*) orbitals at the adjacent carbon atoms $C_{(3)}$ and $C_{(4)}$.

It is not at first evident that a large group such as CCl_3 can replace the hydrogen atom H_α whose proximity to the metal atom is suggested above as the cause of the unusual behaviour of the C–H stretching frequency. However, the cyclopentadiene group is not necessarily planar or parallel to the π-cyclopentadienyl ring, and rough calculations based on simple models for the structure show that large groups substituted in this position on $C_{(1)}$ can be accommodated by a bending of the 1,2- and/or 1,5-bonds, or by a pivoting of the whole C_5 ring, although such groups may not be able to rotate freely about the $C_{(1)}$–C axis.

[Added in proof]: recently, in this laboratory, Dr. R. Watterson has prepared the compound π-C_5H_5(1-*endo*-CF_3·C_5H_5)Co by the reaction between cobaltocene and trifluoromethyl iodide. It is a blood-red oil at ~20° and decomposes only slowly in air. Its proton resonance spectrum is very similar to that of the trichloromethyl derivative, with lines at 5·01 p.p.m. (triple, $H_{(3)} + H_{(4)}$), 4·48 p.p.m. (single, C_5H_5), and 2·34 p.p.m. (quadruple, $H_{(2)} + H_{(5)}$). However, the resonance of H_β, which is centred at 3·08 p.p.m., shows an additional splitting from the three equivalent fluorine (^{19}F) nuclei in the CF_3 group, and appears as a symmetrical quartet (1 : 3 : 3 : 1) of triplets (1 : 2 : 1). The separation between components is 7·4 ± 0·2 c.p.s. in the quartet and 2·4 ± 0·2 c.p.s. in each triplet. The fluorine resonance, which is split by H_β, is a doublet with the same separation (7·3 ± 0·2 c.p.s.).

Experimental

Microanalyses by the Microanalytical Laboratory, Imperial College. Preparations, reaction, and chromatographic separations were carried out in nitrogen or in a vacuum; solvents were degassed before use. Light petroleum is " AnalaR " material of b. p. <40°.

π-Cyclopentadienyl(cyclopentadiene)rhodium.—Preparation. (*A*) Rhodium trichloride trihydrate (7 g., 0·03 mole) (no product was obtained from the insoluble anhydrous halide) was added to a freshly prepared solution of sodiocyclopentadiene [1] (0·2 mol.) in tetrahydrofuran (250 ml.) under nitrogen; the mixture was stirred under reflux for 2 hr. Solid sodium borohydride (5 g.) was added in small portions and after 2 hours' refluxing the solvent was removed. Sublimation from the dry reaction mixture in a vacuum at 130° gave orange-yellow crystals.

Without addition of the borohydride the material was obtained in much lower yield and contaminated with oil which was not readily removed. The product from the borohydride reaction was purified by chromatography on alumina with light petroleum as eluant, and by crystallisation from isopentane (yield ~40% based on rhodium) [Found: C, 51·4; H, 5·0; Rh, 44·3%; *M* (isopiestic in ether with azobenzene as standard) 233, (ebullioscopic in benzene) 233. $C_{10}H_{11}Rh$ requires C, 51·3; H, 4·7; Rh, 43·95%; *M*, 234·1].

(*B*) A solution of rhodicenium chloride [6] (0·5 g.) was evaporated to dryness in a vacuum and the residue was dissolved in 80% ethanol (5 ml.). Sodium borohydride (~2 g.) was added in portions; after ½ hr. the solvent was removed and the oily residue extracted with light

[16] Dewar, *Bull. Soc. chim. France*, 1951, **18**, C71; Chatt and Duncanson, *J.*, 1953, 2939.

petroleum. After drying, the solution was evaporated and the product recovered by vacuum-sublimation in ~80% yield.

Properties. The compound decomposes in air, only about 50% being recoverable after 2 days. It is soluble in benzene, light petroleum, and similar organic solvents; these solutions decompose within a few hours in air, and even in absence of air the benzene solutions darken in a few days, presumably owing to photochemical decomposition. The compound has a strong camphoraceous odour and readily sublimes in a vacuum at 50°. It is stable indefinitely in absence of air.

In carbon tetrachloride solution, decomposition sets in within a few minutes; infrared spectra show that chloroform and one or more olefins are formed. The precipitate obtained on treatment with water or dilute acids gives a solution of the rhodicenium ion. Carbon disulphide solutions also decompose quite rapidly, but the products have not been studied. With carbon monoxide at 100°/250 atm. extensive decomposition occurs.

With 3N-hydrochloric acid (5 ml.) the compound (7·755 mg.) gave 218 ml. of gas (at N.T.P.). Of this 50% was hydrogen. The infrared spectrum of the remainder showed peaks at 3080m, 2950s, 2870s, 1625m, 1458m, 1447m, 1345w, 1287w, 1215w, 1060w, 1047m, 1030m, 918w, 896m, 708m, 693s, 675m, among which bands due to C=C, $=CH_2$, and $-CH=CH_2$ groups can be recognised. Mass-spectrography showed that the main constituent had mass 68; a trace (0·2%) of butenes was also present.

π-Cyclopentadienyl(cyclopentadiene)cobalt.—Anhydrous cobalticenium tribromide (5 g.) (prepared in the same way as the methyl derivative below but from sodiocyclopentadiene [1]) in 1,2-dimethoxyethane (150 ml.) was treated with an excess of sodium borohydride (5 g.) in small portions with stirring. Hydrogen was evolved and a green coating formed on the sodium borohydride (probably cobalticenium borohydride). On warming to 60°, or on addition of water (2 ml.), the mixture became deep wine-red. After 1 hr., the solution was filtered and the residue washed with the ether. (If the solution is not filtered at this stage, sublimation of the dried mixture gives a high yield of the purple-black cobaltocene; reduction of the cobalticenium ion with lithium aluminium hydride in this way has previously been shown to give cobaltocene.[17]) The filtrate was reduced to a few ml. in a vacuum and extracted with light petroleum. This solution was concentrated and the product separated on a 20-cm. alumina column. The first red band eluted by light petroleum was evaporated and the residue sublimed in a vacuum to a probe at −70° to give the product (yield 80%) [Found: C, 63·0; H, 6·2%; *M* (ebullioscopic in benzene), 193. $C_{10}H_{11}Co$ requires C, 63·2; H, 5·8%; *M*, 190]. The compound is less stable than the rhodium analogue. It can be handled in air only for a few minutes and in organic solvents rapidly decomposes on exposure to air; even degassed solutions in organic solvents show notable decomposition within a few hours. The compound is more volatile than the rhodium compound and has a similar odour. The reactions with aqueous acid and carbon tetrachloride are similar to those of the rhodium analogue.

The Deutero-compound, π-$C_5H_5(C_5H_5D)Co$.—To a solution of lithium aluminium deuteride (0·2 g.) (Metal Hydrides Inc., Beverley, Mass.) was added solid anhydrous cobalticenium chloride in small portions until no effervescence occurred. The product was isolated as above (yield, ~80% based on $LiAlD_4$). An estimate of the isotopic purity by infrared measurements gave over 90% deuterium.

The anhydrous cobalticenium chloride was obtained by evaporating hydrochloric acid solutions on a steam-bath to give a dark green oil. This was triturated with tetrahydrofuran, and the residual crystals were then dissolved in and crystallised from tetrahydrofuran; it forms large pale green crystals and is as an etherate.

Equilibration of $C_{10}H_{11}Co$ *with* $LiAlD_4$.—The cobalt compound (~0·05 g.) was set aside in tetrahydrofuran solution at 25° with an excess of $LiAlD_4$. After 3 hr. the solvent was removed and the compound extracted and purified. The infrared spectrum was identical with that of the starting material.

Preparation of 1,1′-Dimethylcobalticenium Salts.—To sodiomethylcyclopentadiene [18] (1·0 mole) in tetrahydrofuran (300 ml.) was added anhydrous cobaltous chloride (0·5 mole). After 2 hours' stirring at the b. p. the solvent was removed and the residue treated with 1 : 1 hydrochloric acid (100 ml.). The yellow aqueous layer was separated, washed twice with ether, and filtered. To a portion of the filtrate was added a solution of Reinecke's

[17] Birmingham, Fischer, and Wilkinson, *Naturwiss.*, 1955, **42**, 96.
[18] Reynolds and Wilkinson, *J. Inorg. Nuclear Chem.*, 1959, **9**, 86.

salt; the pale pink *salt* precipitated was centrifuged, washed, and dried {Found: C, 34·7; H, 3·6. $[C_{12}H_{14}Co][Cr(NH_3)_2(SCN)_4],H_2O$ requires C, 34·6; H, 3·9%}. The remainder of the solution was treated with bromine water and the precipitated tribromide was removed and dried at 80° in a vacuum to leave a pale yellow powder.

π-Methylcyclopentadienyl(methylcyclopentadiene)cobalt.—This *compound* was prepared from the tribromide as for the unsubstituted compound. On evaporation of the eluate from the chromatographic column, a deep red oil was obtained. On an 80-cm. alumina column, further treatment gave only a single sharp elution band. The oil melted sharply at ~−5°; it was purified by vacuum-distillation (Found: C, 65·1; H, 6·8. $C_{12}H_{15}Co$ requires C, 66·0; H, 6·9%).

π-Cyclopentadienyl(1-endo-methylcyclopentadiene)cobalt.—Cobaltocene [1] (3 g.) and methyl iodide (5 ml.) were heated in a sealed tube at 80° for 2 hr. The excess of methyl iodide was then removed and the residue extracted with a 7 : 3 mixture of light petroleum (b. p. 40—60°) and anhydrous ether. The *product* was chromatographed twice with the petroleum–ether mixture as eluant; it was finally distilled at 40°/10^{-3} mm. to an ice-cooled probe to give a red oil (yield, ~30% based on $C_{10}H_{10}Co$; theor., 50%) [Found: C, 64·7; H, 6·4%; *M* (ebullioscopic in benzene), 204. $C_{11}H_{12}Co$ requires C, 64·8; H, 6·7%; *M*, 204·6].

Reaction of cobaltocene with methyl iodide was very slow at room temperature, no product being isolated after 12 hr., and ultraviolet irradiation did not increase the reaction rate.

The compound is readily soluble in all organic solvents, but the solutions and the pure compound decompose in air fairly rapidly to give traces of paramagnetic species, as shown by loss of nuclear magnetic resonance resolution.

π-Cyclopentadienyl(1-endo-trichloromethylcyclopentadiene)cobalt.—Cobaltocene (3 g.) was treated with carbon tetrachloride (5 ml.); after 1 hr. the tetrachloride was removed and the residue extracted with light petroleum (b. p. 40—60°). After chromatography with light petroleum–ether the eluate was evaporated and the *product* (45% based on $C_{10}H_{10}Co$) crystallised at low temperatures from isopentane [Found: C, 43·2; H, 3·7%; *M* (ebullioscopic in benzene), 306. $C_{11}H_{10}Cl_3Co$ requires C, 42·9; H, 3·2%; *M*, 307·6]. It is considerably more stable than its methyl analogue and is freely soluble in organic solvents; carbon tetrachloride solutions are stable in air for 24 hr.

π-Cyclopentadienyl(1-endo-dichloromethylcyclopentadiene)cobalt.—π-Cyclopentadienyl-(1-*endo*-trichloromethylcyclopentadiene)cobalt (0·5 g.) in tetrahydrofuran was treated with an excess of lithium aluminium hydride (1·0 g.). After ½ hr. a large excess of water was carefully added to the mixture, and the solution extracted with light petroleum. The orange petroleum layer was separated, washed thoroughly with water, dried ($CaCl_2$), and evaporated to a small volume which was chromatographed in ether–petroleum on a 3 ft. alumina column. The eluate was evaporated and the *product* (75%) crystallised at low temperatures from isopentane [Found: C, 48·6; H, 4·3; Cl, 26·1%; *M* (ebullioscopic in benzene), 278·7. $C_{11}H_{11}Cl_2Co$ requires C, 48·4; H, 4·1; Cl, 26·0%; *M*, 273]. It is very similar to the 1-*endo*-trichloromethyl analogue.

Infrared Spectra.—Measurements were made with a Perkin–Elmer Model 21 spectrometer with sodium chloride and calcium fluoride optics. High-resolution spectra in the 2500—3200 $cm.^{-1}$ region were obtained by using a modified Grubb–Parsons instrument with lithium fluoride optics. The compounds were run in carbon tetrachloride and carbon disulphide; although the $C_{10}H_{11}M$ compounds decompose in these solvents, consecutive spectra taken in a 10-minute period immediately after preparation of the solution were the same. Spectra were also taken in tetrachloroethylene and in 1,1,2-trichlorotrifluoroethane which do not react as rapidly as the above solvents. The spectrum of the methyl derivatives was taken on a thin film of the pure liquid.

Details of the spectra (excluding bands listed in Table 2) are:

π-$C_5H_5(C_5H_6)Co$ (in CS_2 and C_2Cl_4), 3880w, 3720vw, 2440w, 2380w, 1737w, 1700w, 1664w, 1609w, 1518m, 1443w, 1412w, 1384w, 1370w, 1350w, 1330w, 1240m, 1107m (π-C_5H_5), 1066m, 1037w, 1006s (π-C_5H_5), 993m, 984m, 920m, 810s (π-C_5H_5), 780s.

π-$C_5H_5(C_5H_5D)Co$ (in CS_2 and C_2Cl_4), 3900w, 1964w, 1945w, 1775w, 1742w, 1705w, 1665w, 1590w, 1426w, 1412m, 1372w, 1336m, 1301m, 1251w, 1245w, 1216m, 1105m (π-C_5H_5), 1070s, 1046m, 1010s (π-C_5H_5), 996s.

π-$C_5H_5(C_5H_6)Rh$ (in CS_2 and $CF_2Cl{\cdot}Cl_2F$), 3860w, 2462w, 2425w, 2040w, 1820w, 1765w, 1665m, 1384m, 1372m, 1345m, 1335m, 1252m, 1234m, 1105s (π-C_5H_5), 1065s, 1034m, 1006s (π-C_5H_5), 995s, 923m, 898w, 865m, 828vw, 822s (π-C_5H_5), 785vs.

π-Me·C_5H_4(Me·C_5H_5)Co (pure liquid and in CS_2), 3860w, 3095m, 3056m, 2935s, 2885s, 2720s, 2050vw, 1474m, 1445s, 1416m, 1374m, 1363m, 1340w, 1264m, 1230w, 1188w, 1107w, 1035s, 998m, 1067w, 934w, 920m, 780m.

π-C_5H_5(1-*endo*-CH_2·C_5H_5)Co (pure liquid and in CS_2), 3850w, 2760vw, 1764vw, 1659vw, 1612vw, 1587vw, 1451m (CH_2 def.), 1415m, 1385w (CH_2 def.), 1355w, 1342w, 1317m, 1272vw, 1254w, 1126m, 1100m (π-C_5H_5), 1055w, 1036m, 1024m (π-C_5H_5), 929vw, 917vw, 868w, 858w, 825s (π-C_5H_5), 790vw, 726vw.

π-C_5H_5(1-*endo*-$CHCl_2$·C_5H_5)Co (in CCl_4 and CS_2), 3100m, 3080m, 2962s, 2946s, 2880m, 1752w, 1710w, 1377w, 1348w, 1330w, 1314w, 1262vw, 1220m, 1187w, 1105w (π-C_5H_5), 1065w, 1042w, 1009m, 996m (π-C_5H_5), 823s, 806s (π-C_5H_5), 794s, 739m, 725w, 698m.

π-C_5H_5(1-*endo*-CCl_3·C_5H_5)Co (in CCl_4 and CS_2), 1872w, 1788w, 1741w, 1692w, 1640w, 1577w, 1385w, 1380w, 1351w, 1343w, 1292m, 1214m, 1166m (π-C_5H_5), 1072m, 1049m, 1010s, 1001s (π-C_5H_5), 912s, 1844s, 863s (π-C_5H_5), 757m, 732s.

Nuclear Magnetic Resonance Spectra.—The spectra at 40 Mc./sec. were obtained on a Varian Associates Model 4300B spectrometer; spectra at 60 Mc./sec. were obtained on a similar instrument through the courtesy of the Varian staff at the Brussels World Exhibition. Measurements were made at 22° ± 2° in strong solutions in benzene and cyclohexane contained in spinning tubes of 5 mm. outside diameter. A small amount of tetramethylsilane was added to each sample as an internal reference. Line positions were measured by the conventional side-band technique.

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761. *The Solubility of Alkali Metals in Ethers.*

By J. L. DOWN, J. LEWIS, B. MOORE, and G. WILKINSON.

Potassium and sodium–potassium eutectic dissolve slightly (of the order of 10^{-4} g.-atom/l.) in certain ethers to give unstable blue solutions which are considered to be similar to the well-known blue solutions of alkali metals in ammonia and amines. Absorption spectra of the solutions show maxima at about 7000 Å.

An attempt has been made to correlate the ability to give a blue solution with the structure and basicity of the ethers.

IT has previously been reported [1] that moderately stable blue solutions of potassium and sodium–potassium alloy in some ethers may be obtained. Solubility has since been observed in some fifteen ethers and one amino-ether. The solutions are immediately decolorised by air but they can be filtered through a sintered-glass disc *in vacuo*. Filtered solutions decolorise at room temperature, rapidly in some cases and slowly in others, owing principally to attack on the solvent by the alkali metal. The nature of the decomposition products has not been investigated. Generally, the total alkali-metal concentration appears to increase with decrease in temperature; in some ethers, *viz.*, the dimethyl ethers of polyethylene glycols, the surface of the sodium–potassium alloy exhibits a copper-coloured lustre at low temperature, presumably on account of the formation of alkali-metal

[1] Down, Lewis, Moore, and Wilkinson, *Proc. Chem. Soc.*, 1957, 209 (where references to previous work with water and alcohols are given).

etherates, analogous to the copper-coloured ammoniates formed on evaporation of liquid ammonia solutions of alkali metals.[2]

Results and Discussion

The extent of the solubility of potassium and sodium–potassium alloy in various ethers and amines as estimated visually from the intensities of the blue colorations is shown in Table 1; the dielectric constant and the basicity (as determined by O–D shifts) of certain ethers are also cited.

The only metals which have been found to give blue solutions are potassium and sodium–potassium alloy; at a given temperature the alloy solutions were always more intensely coloured than the solutions with potassium alone but this may possibly be a surface effect since the liquid alloy always presents a clean surface. Sodium is found in the blue solutions, however, but in view of the low total metal solubility ($\sim 10^{-4}$ g.-atom/l.) it is difficult to be certain that this may not be due to attack on the solvent either by the metal or by traces of oxides leading to the formation of soluble sodium salts such as alkoxides. It may be noted, however, that Ubbelohde [3] did not report a blue coloration when sodium was stimulated ultrasonically in ethylene glycol dimethyl ether; further, we have detected no sodium in a blue solution obtained from frozen sodium–potassium alloy.

Lithium, sodium, and calcium have failed to give blue solutions even in the most favourable ethers; since it is very difficult indeed to obtain clean surfaces of the metals, this result may not be conclusive, although in the case of sodium the experiment by Ubbelohde (noted above) strongly suggests that sodium is indeed insoluble in ethylene glycol dimethyl ether. Since some of the factors noted below, particularly the solvation effect, would have been expected to favour the solubility of the lighter alkali metals, it seems reasonable to attribute the failure to dissolve in the ethers, which are of course of rather low dielectric constant, to the higher ionisation potentials; we hence predict that rubidium and cæsium will give blue solutions, although the rate of attack on ethers may be high.

It seems reasonable to assume that, as in liquid ammonia and amines, the metal atoms dissolved in ethers are dissociated to give " solvated " electrons and solvated cations. The solubility will thus depend to a large extent on the ability of the solvent molecules to stabilise such species in solution.

The various factors which could influence the solubility properties of a given series of ethers are as follows: (1) The donor power of the oxygen atom; here, differences in the electron-donor ability are reflected in changes in the position of the O–D stretching frequency in the infrared spectra of solutions of $CH_3 \cdot OD$ in the ethers.[4] (2) The dielectric constant of the ether. (3) The number of oxygen atoms in the ether. (4) The size of the ring formed in a chelated solvate of a cation. (5) Steric interaction by substituents near to the oxygen atom of the ether. (6) Stability of the solvent towards reduction by " solvated " electrons.

Certain of these factors are obviously inter-related. However, the major factors that appear to influence the solubility of the metal in ethers are (3), (4), and (5), and it seems that to a large extent the factors are those relating to solvation of the alkali-metal ion. Of course, the criteria for solvation of the electron, which would also provide a driving force for the solubility, are considerably more difficult to discern. Most of the ethers which give blue solutions contain more than one oxygen atom; co-ordination of the oxygen atom to a metal ion in solution would lead to the formation of five-membered chelate rings, and the solubility may be associated with this effect. It is well known that steric effects play an important part in complex formation generally; in the present case, the

[2] Ruff, *Ber.*, 1901, **34**, 2604.
[3] Slough and Ubbelohde, *Proc. Chem. Soc.*, 1957, 918.
[4] Gordy, *J. Chem. Phys.*, 1939, **7**, 93.

presence of bulky substituents near the oxygen atoms clearly decreases the ability of the ethers to dissolve metals, even though little or no change in the basicity of the ether is involved.

TABLE 1. *Solubilities of metals in various solvents.*

Solvent	Dielectric constant	O–D shift ($cm.^{-1}$)	Metal	Colour at room temp.
Dimethyl ether	7·4		Na–K	None
Diethyl ether	4·22	95	Na–K	None
Di-isopropyl ether		106	Na–K	None
Ethylene glycol ethers				
Dimethyl	5·50	92	Na–K	Intense
,,			K	Moderate
,,			Na	None
,,			Li	None
,,			Ca	None
,,			K/Hg	Blue surface on amalgam
,,			Na/Hg	None
,,			NaK/Hg	Blue surface on amalgam
Ethyl methyl		91	Na–K	Pale
Diethyl	5·10	88	Na–K	None
Methyl n-propyl		93	Na–K	None
n-Butyl methyl		92	Na–K	None
Diethylene glycol ethers				
Dimethyl	5·79	94	Na–K	Intense
Diethyl	5·70	91	Na–K	Pale
Ethyl methyl		93	Na–K	Moderate
Methyl n-propyl				Pale [a]
n-Butyl methyl	5·34	94	Na–K	Very pale [a]
Cyclic ethers				
Tetrahydropyran	5·44		Na–K	None
Tetrahydrofuran	6·00	112	Na–K	Pale
1-Methoxymethyltetrahydrofuran		106	Na–K	Intense
1-Ethoxymethyltetrahydrofuran		103		Moderate [b]
1-Propoxymethyltetrahydrofuran			Na–K	None
2-Methyltetrahydrofuran	4·63		Na–K	Very pale [a]
Dioxan	2·23		Na–K	None
Trimethylene oxide		114	Na–K	None
Cyclic tetramer of propylene oxide		114	Na–K	Intense
Miscellaneous				
1 : 2-Dimethoxypropane		94	Na–K	Very pale [a]
1 : 3-Dimethoxypropane	5·48	95	Na–K	None
2 : 3-Dimethoxybutane		96	Na–K	None
1 : 2 : 3-Trimethoxypropane		95	Na–K	None
Triethylene glycol dimethyl ether		95	Na–K	Very intense
Tetraethylene glycol dimethyl ether			Na–K	Very intense
Pentamethylene glycol dimethyl ether	5·27		Na–K	None
Amines				
Diethylamine	3·7		Na–K	None
Triethylamine	3·15		Na–K	None
Ethylenediamine	16·0		Na–K	Very intense
Methoxyethylamine			Na–K	Very intense

[a] Only on prolonged cooling to 193° K. [b] Pale at room temperature; moderate on cooling to 193° K.

(a) *Simple and cyclic monoethers.* The fact that no alkali-metal solutions have been obtained in dialkyl monoethers is probably due to steric hindrance in formation of a cation solvate as compared with cyclic monoethers. This comparison has been made in a different context by Ferguson.[5] No solubility was observed in tetrahydropyran and dioxan, where the oxygen atoms have lower electron-donor abilities than those in trimethylene oxide and tetrahydrofuran.[6]

[5] Ferguson, *J. Amer. Chem. Soc.*, 1955, **77**, 5289.
[6] Searle and Tamres, *J. Amer. Chem. Soc.*, 1951, **73**, 3704.

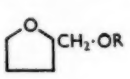
(b) *Ethylene glycol ethers*, $RO{\cdot}CH_2{\cdot}CH_2{\cdot}OR'$. When R = R′ = Me, deep-blue solutions may be obtained, but replacement by R = R′ = Et results in no solubility, presumably owing to steric hindrance. The intermediate ether where R = Me, R′ = Et, gives a solution of intermediate colour intensity. If R = Me and R′ = Pr^n or Bu^n, no blue solution is obtained, indicating that one of the oxygen atoms is sufficiently " shielded " to prevent chelate-ring formation. Further evidence of steric inhibition is seen when the solubility is lowered as one, and then two, methyl groups are introduced into the $-CH_2{\cdot}CH_2-$ chain in ethylene glycol dimethyl ether.

(c) *Ethers of diethylene glycol*, $RO{\cdot}CH_2{\cdot}CH_2{\cdot}O{\cdot}CH_2{\cdot}CH_2{\cdot}OR'$. The ethers in this series will behave as tridentate ligands, giving rise to higher solubility than for the ethylene glycol ether when R = R′ = Me. However, successive replacement of one of the terminal methyl groups by Pr^n, Bu^n lowers the tendency to dissolve. When R = R′ = Et, the steric hindrance is not quite large enough to prevent slight solubility.

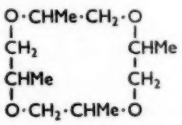
(d) $CH_3{\cdot}[O{\cdot}CH_2{\cdot}CH_2]_n{\cdot}O{\cdot}CH_3$. As n increases from 1 to 4 there is a very marked increase in solubility owing to an increase in the number of donor atoms per ether molecule. Entropy effects of chelation will evidently become more pronounced as n increases.

(e) $CH_3{\cdot}O{\cdot}[CH_2]_n{\cdot}O{\cdot}CH_3$. As would be expected, when $n > 2$, the chelate rings are unstable and no solubility is observed when $n = 3$ and 5.

(f) *Miscellaneous ethers.* Alkoxymethyltetrahydrofurans (I), which combine the low steric hindrance associated with the cyclic ether and the chelation effect due to the presence of a second oxygen atom, give blue solutions, solubility being greatest when R = Me and gradually decreasing to zero when R = Et, Pr^n.



(I)



(II)

The cyclic tetramer of propylene oxide (II) gives a deep-blue solution of appreciable stability. Whilst the chelating possibility of this ether is obviously important, it may be noted that the high viscosity may be responsible in part for the stability of these solutions; the stability of filtered blue solutions in other ethers does indeed appear to be higher for the more viscous ethers.

(g) *Amines.* As would be expected from previous work by Birch,[7] no solubility was observed for diethylamine and triethylamine. This is to be expected since the ease of complex formation decreases in the order $NH_3 > RNH_2 > R_2NH > R_3N$, the last being almost devoid of ability to co-ordinate with metal ions. It seems that steric effects rather than differences in electron-donor ability are mainly responsible for this decrease, since tertiary amines co-ordinate firmly with the hydrogen ion. The observation that lithium does not dissolve in dimethylamine, although it is quite soluble in the isomeric ethylamine, is further evidence of the importance of steric effects in the solubility property towards alkali metals.

It is noteworthy that 2-methoxyethylamine gives intensely coloured solutions.

Absorption Spectra.—The absorption spectra of blue solutions of potassium and sodium–potassium alloy in some ethers (Table 2) were measured in the wavelength region 22,000—6000 Å; all spectra showed only a well-defined maximum at about 7000 Å. The positions of the maxima did not alter with changes in temperature or concentration. The spectrum of potassium in ethylene glycol dimethyl ether showed a small shoulder at 8290 Å.

Solutions of alkali metals in ammonia and amines show one or both of two very intense absorption bands—one in the visible (~6500 Å) and the other in the infrared (~15,000 Å) region. Solutions showing the former are diamagnetic while those showing the latter are

[7] Birch and MacDonald, " Oxford Science," 1948, **1**.

paramagnetic. It has been suggested [8,9] that in such solutions, paired and unpaired "solvated" electrons, respectively, exist in cavities. At the same time it has been observed that in solutions showing both absorption bands, there is evidence to indicate that an equilibrium exists between the two electronic species.

For solutions of alkali metals in ethers, no bands were observed in the region 13,000—18,000 Å, which corresponds to the e_1 type cavities in ammonia and amine solutions. Such solutions would therefore be expected to be diamagnetic. Although we observed no

TABLE 2. *Absorption spectra of blue solutions in ethers.*

Ether	Metal	$\lambda_{max.}$ (Å)
Ethylene glycol dimethyl ether	Na–K	7075
" "	K	7290, 8290 (sh)
Tetrahydrofuran	Na–K	7050
1-Methoxymethyltetrahydrofuran	Na–K	7150
" " "	K	7170
Diethylene glycol dimethyl ether	Na–K	6990
2-Methoxyethylamine	Na–K	7170
" "	K	6800

paramagnetic resonance signals from a frozen blue solution of sodium–potassium alloy in ethylene glycol dimethyl ether at temperatures down to 90° K, Weissman [10] reports a weak spin resonance absorption line, about 2 œrsteds in breadth, from a solution of potassium in the same solvent at 193° K.

Solubility Measurements.—Attempts have been made to determine the solubilities of potassium and sodium–potassium alloy in ethylene glycol dimethyl ether, and also that of this alloy in tetrahydrofuran, 1-methoxymethyltetrahydrofuran and diethylene glycol dimethyl ether. Initially, the determinations were made by measuring the alkali-metal content by using a flame photometer. The solubility is in all cases very low and we cannot consider the measurements reliable since the total alkali content possibly included unknown contributions arising from soluble decomposition products of the ether and from oxides in the metals. Hence a few solubilities were determined by measuring the volume of hydrogen evolved when a blue solution was decomposed by water.

We conclude that the maximum upper limit of the solubilities is of the order of 10^{-4} g.-atom/l. for each alkali metal. There is some evidence to suggest that potassium has a negative, and sodium a positive, temperature coefficient of solubility. This is in agreement with the solubilities of these metals in ammonia. Furthermore, the solubility of potassium alone in ethylene glycol dimethyl ether appears to show a shallow minimum at about −30° C. The attack on the ether would increase with temperature, and the general shape of the curve of the apparent solubility of potassium in ethylene glycol dimethyl ether could arise from a concomitant increasing decomposition and decreasing solubility with temperature.

EXPERIMENTAL

As the solutions were unstable to air they were handled *in vacuo* or in oxygen-free nitrogen, methods similar to those described previously [8] being used.

Preparation and Purification of Materials.—Solvents. Several ethers were available commercially. Others were prepared from available hydroxy-compounds by the Williamson method. The products were fractionally distilled, freed from alcohols by refluxing them over sodium, and distilled from lithium aluminium hydride in a stream of nitrogen.

The cyclic tetramer of propylene oxide was prepared by polymerisation with boron trifluoride–ether complex, according to a method kindly provided by Mr. W. J. Toussaint of Union Carbide Chemicals Co., which is as follows: Dry propylene oxide (2198 g.) was added to a flask equipped with a stirrer, a brine-cooled condenser, and a feed tank for catalyst addition. The

[8] Fowles, McGregor, and Symons, *J.*, 1957, 665, 3329.
[9] Ogg, *J. Chem. Phys.*, 1946, **14**, 114.
[10] Weissman, *J. Amer. Chem. Soc.*, 1958, **80**, 5342.

propylene oxide was heated under reflux while being stirred. The catalyst [boron trifluoride–ethyl ether complex (47% BF_3, 56 g.)] was fed in during 7 hr. at such a rate as to maintain vigorous boiling without application of external heat. The crude product was boiled for 2 hr., the final flask temperature being 68°. Unchanged propylene oxide and ethyl ether were removed by distillation to a head temperature of 33° at 180 mm., to a flask temperature of 80°. The boron trifluoride in the crude product was neutralised by stirring and heating it at 85° for 2 hr. with sodium hydroxide solution (75 g. in 500 ml. of water). The lower layer was removed while hot. The product was washed twice at 85° with 250-ml. portions of water, the heated lower layer being removed each time. The remaining water was removed by distillation up to 75° at 34 mm. with a flask temperature of 120°. The tetramer was separated from low- and higher-boiling fractions by distillation through a 1″ × 18″ column of stainless-steel protruded packing. The fractions boiling at 94—122°/5 mm. were collected, combined, and redistilled (yield 38%). The main tetramer fraction was taken at 104·8—105·5°/5 mm.

Amines were dried by refluxing them over potassium hydroxide pellets and then over sodium.

Metals. Since lithium cannot be distilled *in vacuo* in glass apparatus, samples were cut from the centre of a large piece under light petroleum and transferred to the apparatus against a stream of nitrogen. Sodium and potassium were cut from the centre of large pieces under light petroleum and inserted into the apparatus against a stream of nitrogen. The metals were then melted, degassed, and distilled *in vacuo*.

The sodium–potassium eutectic (75% potassium w/w) was transferred in nitrogen, degassed by heating *in vacuo*, and filtered through a plug of glass wool.

Preparation of Blue Solutions.—The solvents were distilled *in vacuo* in a previously degassed apparatus. Solvents were condensed on to sodium and potassium, but in the case of sodium–potassium alloy this was added to the solvents by rotating the bulb containing it around a ground-glass joint. The sample bulb, containing alkali metal and solvent, was then sealed off, and the blue solution obtained by shaking and cooling as necessary.

Measurement of Absorption Spectra.—The absorption spectra were measured *in vacuo* in a 1-cm. fused silica cell fitted with a graded silica-to-Pyrex seal, a Perkin-Elmer Model 4000 recording spectrophotometer being used. The pure solvent was used as the reference liquid. The blue solutions were filtered through a sintered disc into the cell, which was placed in a conventional Dewar system for work at low temperatures.

Solubilities.—The apparatus used to generate blue solutions was immersed in a large Dewar vessel, containing a suitable refrigerant. The solutions were kept in the bath for a standard time of 30 min., being removed periodically and shaken vigorously; they were then filtered through a sintered disc into a bulb. The filtrate was weighed and evaporated to dryness, and the residue made up to 100 ml. with 1% sulphuric acid. The alkali content was determined with an EEL flame photometer calibrated with standard sodium and potassium sulphate solutions in 1% sulphuric acid.

For the determination of the hydrogen evolved, the solvent was degassed *in situ* by melting and freezing it at least ten times. The pressure was measured before and after condensation of degassed water on to the filtrate, frozen at 77° K, by a McLeod gauge.

The following solubilities (in g.-atoms/l. × 10^4) were found. (*a*) By the hydrogen method at 0° in ethylene glycol dimethyl ether, 1 (K), 4 (Na–K); in tetrahydrofuran, 2 (Na–K); these values were the mean of four determinations, the spread being about 2. (*b*) By the flame photometer method: for K in ethylene glycol dimethyl ether: 23°, 4; 0°, 2; −23°, 1; −35°, 2; −48°, 2; −65°, 4; for Na–K in ethyl glycol dimethyl ether: 20°, 4 (Na), 5 (K); 10°, 8 (Na), 10 (K); 0°, 8 (Na), 6 (K); −13°, 8 (Na), 5 (K); −23°, 13 (Na), 3 (K); for Na–K in tetrahydrofuran: 0°, 6 (Na), 3 (K); for Na–K in 1-methoxymethyltetrahydrofuran: 21°, 8 (Na), 2 (K); for Na–K in diethylene glycol dimethyl ether: 21°, 100 (Na), 160 (K).

Dielectric Constants.—These were determined in the standard manner, benzene being used as a reference.

O–D *Shifts.*—These were determined by Gordy's method.[4] CH_3·OD was prepared by the hydrolysis of magnesium methoxide with deuterium oxide. The positions of the O–D peaks in the infrared spectra of approximately M-solutions of CH_3·OD in the ethers were measured by using a Perkin-Elmer Model 21C recording infrared spectrophotometer, equipped with calcium fluoride optics. A 0·1M-solution of CH_3·OD in carbon tetrachloride was taken as a reference. The O–D peak in the reference solution occurred at 2691 $cm.^{-1}$, the spectrum being calibrated by means of the carbon dioxide peak at 2350 $cm.^{-1}$.

Preparative Use of Sodium–Potassium Alloy in Ethylene Glycol Dimethyl Ether.—Solutions of this alloy may be used in preparative chemistry. The alloy is injected into a three-necked flask containing ethylene glycol dimethyl ether under a nitrogen atmosphere. If a blue solution is not formed immediately, cooling in carbon dioxide–acetone produces the required solution. Reactions which are normally carried out by using sodium shot or sodium amalgam in ethers or other inert solvents, usually take place more rapidly in the alloy–ether medium.

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762. *Vapour Pressures of Metal Alkoxides. Part III.*[1] *Hafnium Tetra-t-butoxide and -t-pentyloxide.*

By D. C. BRADLEY and J. D. SWANWICK.

The vapour pressures of hafnium tetra-t-butoxide and -t-pentyloxide have been measured over the range 0·05—50 mm. Hg by the static method. These results were confirmed by hypsometric measurements at pressures >8·0 mm. It is shown that for t-butoxides and t-pentyloxides the order of volatilities is Hf > Zr > Ti over the pressure range studied. From the vapour-pressure equations it is deduced that the molar heats of vaporisation are markedly temperature-dependent. The significance of these results is discussed.

IN previous papers we reported vapour-pressure measurements on the t-butoxides and t-pentyloxides of titanium [2] and zirconium,[1] in which we used an elaborate technique for studying compounds which are extremely readily hydrolysed and susceptible to thermal decomposition. These results proved that the zirconium compound was more volatile than its titanium analogue over a wide range of pressures. In view of the possibility of separating hafnium and zirconium by distillation of their alkoxides, it was necessary to obtain accurate data on the hafnium compounds. In addition, these results should be of special interest from the theoretical viewpoint in connexion with the relation between volatility and molecular weight.[3] We now present results for hafnium tetra-t-butoxide and -t-pentyloxide obtained by the same method as for titanium and zirconium derivatives.

EXPERIMENTAL

Hafnium Alkoxides.—These were prepared by essentially the methods reported previously.[4] Hafnium contents were determined by precipitation of hafnium hydroxide (cf. zirconium) followed by ignition to HfO_2. Careful analyses of (i) dipyridinium hafnium hexachloride $(C_5H_6N)_2HfCl_6$, (ii) hafnium isopropoxide solvate $Hf(OPr^i)_4.Pr^iOH$, (iii) hafnium tetra-t-butoxide, and (iv) hafnium tetra-t-pentyloxide established that the zirconium content of the hafnium was <0·5%. In view of the similar volatilities of the hafnium and the zirconium compounds and the accuracy of the measurements, it was considered unnecessary to correct the results for this small zirconium impurity.

Vapour-pressure Measurements.—The static [2] and the hypsometric [1] method were applied as previously described.

Results.—Hafnium tetra-t-butoxide. The results are presented in Table 1. The vapour pressures in italics or in parentheses were not used in computing the vapour-pressure equation (1). Results in italics were obtained by the hypsometric method. The plot of log *P versus*

[1] Part II, Bradley and Swanwick, *J.*, 1959, 748.
[2] Part I, Bradley and Swanwick, *J.*, 1958, 3207.
[3] Bradley, *Nature*, 1954, **174**, 323.
[4] Bradley, Mehrotra, and Wardlaw, *J.*, 1953, 1634.

$1/T$ showed significant curvature, and accordingly the results were fitted to the " three-constant " equation by the least-squares method described before.[2] Values of P (calc.) were obtained from equation (1).

$$\log P \text{ (calc.) (mm.)} = 67{\cdot}1326 - 6082{\cdot}25_5/T - 19{\cdot}3857 \log T \quad . \quad . \quad . \quad (1)$$

For the 22 measurements from 322·6° to 391·7° K used in computing equation (1), the coefficient of variation is ±0·62%, corresponding to a probable error for any individual point of ±0·43%. These results were obtained from three separate experiments. The number of changes of sign in the deviations ΔP [$P - P$ (calc.)] with the results arranged in order of

TABLE 1. *Hafnium tetra-t-butoxide.*

Temp. (°K)	P (mm.)	P, calc.	Temp. (°K)	P (mm.)	P, calc.	Temp. (°K)	P (mm.)	P, calc.	Temp. (°K)	P (mm.)	P, calc.
300·1	(0·06)	0·07	323·8	0·48	$0{\cdot}48_5$	354·0	3·41	3·44	391·1	21·22	21·26
301·1	(0·06)	$0{\cdot}07_5$	329·6	0·73	$0{\cdot}73_5$	354·5	3·53	3·54	391·7	21·89	21·81
302·0	(0·06)	0·08	329·9	0·75	0·75	355·5	3·75	3·75	396·8	(27·79)	26·87
302·3	(0·07)	$0{\cdot}08_5$	332·2	0·89	0·88	357·7	4·25	4·24	404·7	(37·50)	36·52
303·6	(0·08)	$0{\cdot}09_5$	333·2	0·93	0·94	360·3	4·90	$4{\cdot}88_5$	*412·4*	*51·19*	48·35
305·6	(0·11)	0·11	337·5	1·27	$1{\cdot}25_5$	369·8	7·94	8·00	415·3	(55·74)	53·51
306·2	(0·11)	0·12	337·9	$1{\cdot}29_5$	1·29	*371·5*	*8·49*	8·71	*416·0*	*60·55*	56·71
307·2	(0·12)	0·13	338·0	1·29	1·30	*376·4*	*10·81*	11·03	*418·1*	*62·69*	58·86
309·0	(0·14)	0·15	341·6	1·64	$1{\cdot}63_5$	*377·8*	*11·36*	11·79	*442·6*	*144·7*	124·6
312·2	(0·18)	0·20	343·3	1·83	1·82	378·2	12·01	12·01	*444·3*	*153·7*	130·6
315·5	(0·24)	0·26	349·2	2·61	$2{\cdot}60_5$	384·3	15·83	15·85	*457·7*	*229·5*	183·9
322·6	0·44	0·44	349·3	2·64	2·62	*388·2*	*18·71*	18·79			

TABLE 2. *Hafnium tetra-t-pentyloxide.*

Temp. (°K)	P (mm.)	P, calc.	Temp. (°K)	P (mm.)	P, calc.	Temp. (°K)	P (mm.)	P, calc.	Temp. (°K)	P (mm.)	P, calc.
337·6	(0·04)	0·05	364·4	0·37	$0{\cdot}37_5$	408·3	4·77	4·82	435·4	16·19	16·23
338·6	(0·05)	0·05	370·3	0·56	0·56	408·7	4·88	4·92	*437·0*	*16·94*	17·32
340·4	(0·06)	0·06	370·5	0·56	$0{\cdot}56_5$	413·5	6·19	6·20	446·3	(24·98)	24·86
341·6	(0·06)	0·07	370·9	0·58	0·58	414·3	6·30	6·44	448·6	(27·30)	27·09
343·3	(0·07)	0·08	373·8	$0{\cdot}71_5$	0·70	*419·7*	*8·08*	8·27	453·5	(32·45)	32·39
346·2	(0·10)	0·10	378·5	$0{\cdot}94_5$	0·94	*423·0*	*9·33*	9·59	*455·9*	*35·28*	35·26
350·2	(0·14)	$0{\cdot}13_5$	383·3	$1{\cdot}29_5$	1·25	*424·9*	*10·18*	10·43	465·2	(49·34)	48·41
351·0	($0{\cdot}13_5$)	$0{\cdot}14_5$	390·0	$1{\cdot}86_5$	1·84	426·2	11·00	11·04	*467·6*	*53·43*	53·37
354·4	(0·19)	$0{\cdot}18_5$	390·7	1·93	$1{\cdot}91_5$	427·7	11·85	11·77	471·4	(60·74)	59·14
357·4	$0{\cdot}22_5$	0·23	395·7	2·58	2·52	*429·5*	*12·41*	12·71	*475·2*	*68·8*	66·6
361·4	0·31	$0{\cdot}30_5$	398·9	2·97	2·99	432·4	14·33	14·35	477·3	(73·9)	71·0
361·6	0·31	0·31	403·6	3·83	$3{\cdot}81_5$	435·0	16·04	15·97			

ascending temperature is 10, and this confirms the validity of the " three-constant " equation (statistically 12 ± 2 changes of sign are required). In establishing the purity of the alkoxide, many measurements were made in the range 0·05—0·3 mm. and the 11 points shown in Table 1 are some representative examples. In fact the standard deviation of ΔP in this low-pressure region is ±0·016 mm., with the observed vapour pressures predominantly lower than calculated. The four hypsometric readings within the computed range are in reasonable agreement with the calculated values. Vapour pressures at temperatures above 391·7° K are all higher than calculated. This could be due to increasing thermal decomposition with rise in temperature, although this should not appreciably affect the hypsometric measurements. In the case of zirconium t-butoxide the hypsometric determinations agreed with the calculated values up to 448·1° K (159·3 mm.) before similar deviations were encountered. We are thus faced with the alternatives of suggesting either that the hafnium compound begins to decompose significantly at a temperature of 60° lower than the zirconium analogue does or that equation (1) is not suitable for extrapolation to temperatures above 391·7° K. This is important because of the need to predict the relative volatilities of hafnium and zirconium compounds at the higher pressures in connection with the efficiency of the separation by fractional distillation. We did not observe a very marked difference in thermal stability and this fact, coupled with the similar behaviour of zirconium and hafnium t-pentyloxides, suggests that equation (1) is not suitable for extrapolation to higher temperatures. Accordingly, it is suggested that the experimental values of P between 391·7° and 444·3° K are probably more reliable than P (calc.).

TABLE 3. *Titanium, zirconium, and hafnium t-butoxides.*

Temp. (°K)	300		320		340		360		380		400	
	P, calc.	ΔH_v	*P*, calc.	ΔH_v	*P*, calc.	ΔH_v	*P*, calc.	ΔH_v	*P*, calc.	ΔH_v	*P*, calc.	ΔH_v
$Ti(OBu^t)_4$ ...	0·049	15·8	0·25	15·2	1·00	14·7	3·26	14·1	9·04	13·5	21·41	13·0
$Zr(OBu^t)_4$ ...	0·066	15·9	0·34	15·3	1·35	14·8	4·42	14·2	12·30	13·7	29·77	13·1
$Hf(OBu^t)_4$ ...	0·069	16·3	0·36	15·5	1·48	14·7	4·80	13·9	13·05	13·2	30·49	12·4
P_{Zr}/P_{Ti}	1·34		1·34		1·35		1·36		1·36		1·39	
P_{Hf}/P_{Zr}	1·05		1·08		1·09		1·09		1·06		1·02	

TABLE 4. *Titanium, zirconium, and hafnium t-pentyloxides.*

Temp. (°K)	350		370		390		410		430		450	
	P, calc.	ΔH_v	*P*, calc.	ΔH_v	*P*, calc.	ΔH_v	*P*, calc.	ΔH_v	*P*, calc.	ΔH_v	*P*, calc.	ΔH_v
$Ti(OC_5H_{11}^t)_4$	0·117	17·3	0·44	16·8	1·41	16·4	3·89	15·9	9·55	15·5	21·14	15·0
$Zr(OC_5H_{11}^t)_4$	0·126	18·7	0·52	17·8	1·77	16·9	4·98	16·0	12·13	15·1	26·01	14·2
$Hf(OC_5H_{11}^t)_4$	0·134	18·5	0·55	17·7	1·84	17·0	5·24	16·2	12·98	15·5	28·53	14·7
P_{Zr}/P_{Ti}	1·08		1·19		1·24		1·28		1·27		1·23	
P_{Hf}/P_{Zr}	1·06		1·04		1·04		1·05		1·07		1·10	

Hafnium tetra-t-pentyloxide. The results for 4 experiments on this alkoxide are presented in ascending order of temperatures in Table 2 in the same manner as for the t-butoxide. The plot of log *P versus* $1/T$ gave a curve, and the " three-constant " equation (2) was computed from the results in the temperature range 357·4—435·4° K.

$$\log P \text{ (calc.) (mm.)} = 66{\cdot}6423 - 6897{\cdot}19/T - 18{\cdot}7923 \log T \quad . \quad . \quad . \quad (2)$$

The coefficient of variation for the 24 points used in computing equation (2) was ±1·7%, corresponding to a probable error for a single point of ±1·2%. There were 11 changes of sign in ΔP compared with 13 ± 2 required statistically, confirming the validity of equation (2). The nine results in the low-pressure range (0·04—0·2 mm.) are representative of a large number of measurements which gave a standard deviation of ±0·01 mm. in ΔP. The hypsometric results are in reasonable agreement with equation (2). In fact, good agreement between observed and calculated vapour pressures extends up to 467·6° K (53·37 mm.), and it appears that equation (2) may be extrapolated to this point with confidence.

DISCUSSION

The vapour pressures of the t-butoxides and -pentyloxides of titanium, zirconium, and hafnium have now been shown to conform to the " three-constant " Kirchoff–Rankine equation (3), where *a*, *b*, and *c* are constants;

$$\log P = a - b/T - c \log T \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

This equation is a logical development of the simpler Clausius–Clapeyron equation with allowance for the temperature-variation of the molar heat of vaporisation. Therefore our vapour-pressure results suggest that the molar heats of vaporisation (ΔH_v) for these compounds vary considerably with temperature. This has an important bearing on the fact that for these two series of monomeric derivatives the order of volatilities (Hf > Zr > Ti) is the reverse of that expected according to the common belief that increased molecular weight leads to decreased volatility. For example, if the order of molar heats of vaporisation were Ti > Zr > Hf, then the " anomaly " could simply be explained in terms of differences in intermolecular forces. However, this simple view is not supported by the data presented in Tables 3 and 4. Values of ΔH_v (kcal./mole) have been calculated at selected temperatures and are shown with *P* (calc.) and the relative volatilities P_{Hf}/P_{Zr} and P_{Zr}/P_{Ti}.

It is difficult to assess the errors in the ΔH_v data, but bearing in mind the coefficients of variation of *ca.* ±1% for the vapour pressures, we feel that the error in ΔH_v should not exceed 5%. Thus the data in Table 3 show that the molar heats of vaporisation for the t-butoxides are the same within 5% error for titanium, zirconium, and hafnium at each

temperature. Therefore, the order of volatilities cannot be linked in a simple manner with intermolecular forces, especially since at 300° and 320° K the order of ΔH_v, *viz.*, Hf > Zr > Ti, would favour an order of volatility Ti > Zr > Hf. The relative volatility of zirconium and titanium compounds is practically independent of temperature, whereas for hafnium and zirconium the relative volatility appears to have a maximum at about 350° K. In view of our previously expressed doubts concerning the reliability of extrapolating equation (1) to higher temperatures, we are sceptical about this maximum and suggest that the relative volatility remains at *ca.* 1·02—1·05 up to about 500° K instead of falling below unity.

The molar heats of vaporisation for titanium, zirconium and hafnium t-pentyloxides are the same within 5% for each temperature except 350° and 370° K where the order is Hf ~ Zr > Ti. Therefore, the order of volatilities cannot be explained in terms of intermolecular forces and it is clear that an entropy effect [3] is involved. With regard to the relative volatility of zirconium and titanium pentyloxides, a significant temperature-dependence is apparent. Nevertheless, these values are considerably lower than those found for the t-butoxides. For hafnium and zirconium t-pentyloxides the relative volatility is practically constant at *ca.* 1·06 over the whole temperature range.

These results show that in principle it is possible to separate hafnium from zirconium by fractional distillation of either the t-butoxides or the t-pentyloxides under reduced pressure with a column of high efficiency.

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763. *Mechanism and Steric Course of Octahedral Aquation. Part I. Aquation of some Halogeno- and Nitrato-amminebis(ethylenediamine)-cobalt*(III) *Ions.*

By M. L. TOBE.

Rates of aquation of *trans*-[Co en$_2$(NH$_3$)NO$_3$]$^{2+}$, *trans*-[Co en$_2$(NH$_3$)Br]$^{2+}$, and *trans*-[Co en$_2$(NH$_3$)Cl]$^{2+}$ have been measured over a range of temperature, and the Arrhenius parameters determined. In each case the initial product is *trans*-[Co en$_2$(NH$_3$)H$_2$O]$^{3+}$, which slowly isomerises to the *cis*-isomer. In no case was any *cis*-isomer formed directly. A mechanism is discussed in which hydrogen bonding between the incoming and the outgoing ligand is believed to play some part in lowering the activation energy.

AŠPERGER and INGOLD [1] have studied the way in which the electron-displacing properties of the ligand A in complex ions of the type [Co en$_2$ACl]$^+$ (en = ethylenediamine) affect the rate of replacement of the chloride ion by water, and have suggested that the results may be explained by assuming a duality of mechanism. A conjugatively electron-donating group, such as HO or Cl, assists heterolysis of the Co–Cl bond, and promotes a unimolecular mechanism, designated as S_N1. Electron-withdrawing groups, such as H_3N^+ or O_2N, promote a bimolecular process (S_N2). The results indicate, furthermore, that bond-making is now much more important than bond-breaking, so that the transition state can be pictured as one in which both the incoming and the outgoing ligands are almost fully bound to the cobalt atom.

This paper is the first of a series in which these aquations will be examined in detail, in order to gain more insight into the factors controlling their mechanism and steric course. The complexes examined, namely, *trans*-[Co en$_2$(NH$_3$)X]$^{2+}$, where X = Cl, Br, or NO$_3$, are

[1] Ašperger and Ingold, *J.*, 1956, 2862.

expected, according to Ašperger and Ingold's suggestion, to undergo bimolecular aquation. This accords with Adamson and Basolo's suggested mechanism of aquation of chloro- and bromo-pentamminecobalt(III) cations; [2] for the replacement of four ammonia molecules by two molecules of ethylenediamine would not be expected to change the mechanism of the reaction. In the present work, *trans*-isomers were used, in order that the steric course of the reaction could be interpreted unambiguously.[3]

The aquation of *trans*-chloroamminebis(ethylenediamine)cobalt(III) salts has been examined before.[4,5] However, in the first investigation, the kinetics were not studied, and the analysis of the products did not take into account the rearrangement of the products; in the second, the kinetics were studied but no information on steric course was given.

The rate of isomerisation of the aquo-ammine product is dependent upon the pH of the solution, and by studying the aquation in 0·1N-perchloric acid it is possible to reduce the velocity sufficiently for the overall reaction to be treated as two consecutive first-order reactions with similar rate constants. It is then possible to distinguish between any appearance of the *cis*-aquoamminebis(ethylenediamine)cobalt(III) cation as a result of aquation and that formed by the rearrangement of the *trans*-isomer. Such an analysis of the overall reaction into its components, with determination of the steric course of the initial substitution by water, has been completed for the aquations of the *trans*-chloro-, -bromo-, and -nitrato-ammine cations mentioned above.

(1) *Isomerisation of the* trans-*Aquoamminebis(ethylenediamine)cobalt*(III) *Cation in Aqueous Solution.*—*trans*-Aquoamminobis(ethylenediamine)cobalt(III) nitrate, when heated in aqueous solution, rearranges to the *cis*-form. The solution, at equilibrium, contains no spectrophotometrically detectable amount of the *trans*-isomer. Further, an optically active sample of the *cis*-isomer racemises when heated in acidified aqueous solution very much more slowly than the *trans*- is converted into the *cis*-isomer.

The rate at which the *trans*-isomer rearranges in aqueous solution depends upon the concentration of the hydrogen ions. Table 1 gives the rate constants k_2 for the reaction *trans*-[Co $en_2(NH_3)H_2O]^{3+} \longrightarrow$ *cis*-[Co $en_2(NH_3)H_2O]^{3+}$ at different hydrogen-ion concentrations. The rate of isomerisation obeys the kinetic expression

$$-\mathrm{d}[trans]/\mathrm{d}t = 5{\cdot}5 \times 10^{-5}[trans] + 3{\cdot}4 \times 10^{-7}[trans]/[\mathrm{H}^+]$$

for the range $0{\cdot}2\text{N} > [\mathrm{H}^+] > 0{\cdot}002\text{N}$.

This acid-dependence is now being studied in more detail by Dr. D. F. Martin, and it seems that the kinetic form can be attributed to a very easy reaction path *via* the *trans*-hydroxoamminebis(ethylenediamine)cobalt(III) cation. If the pK of the *trans*-aquoamminebis(ethylenediamine)cobalt(III) cation is assumed to be about 6, it would follow that the first-order rate constant for the isomerisation of the *trans*-hydroxoammine complex ion is of the order of 10^{-1} sec.$^{-1}$ at 72·8°.

TABLE 1. *Rate constants for the rearrangement of trans-*[Co $en_2(NH_3)H_2O)]^{3+}$ *at* 72·8°.

[The constant k_2 is obtained from the slope of the plot of log $(D_\infty - D_t)$ against time (t), where D_∞ is the optical density of the solution at 4800 Å, the subscripts referring to the time. The optical density of the solution after 10 half-lives was taken as D_∞ and corresponded very well with that expected for the pure *cis*-isomer.]

$[\mathrm{H}^+]$ (N)	0·201	0·193	0·0426	0·0123	0·0026	no added acid
$10^5 k_2$ (sec.$^{-1}$)	5·3 *	5·6	5·9	7·4	17·2	131 *

* Data refer to the perchlorate except that nitrate was used for this run.

(2) *Aquation of the* trans-*Chloroamminebis(ethylenediamine)cobalt*(III) *Cation.*—(2a) *Kinetics.* Nyholm and Tobe [5] reported rates of aquation of *trans*-[Co $en_2(NH_3)Cl]Cl,ClO_4$

[2] Adamson and Basolo, *Acta Chem. Scand.*, 1955, **9**, 1261.
[3] Brown, Ingold, and Nyholm, *J.*, 1953, 2674.
[4] Basolo, Stone, and Pearson, *J. Amer. Chem. Soc.*, 1953, **75**, 819.
[5] Nyholm and Tobe, *J.*, 1956, 1707.

at two temperatures. Since the reaction does not go to completion, the system was treated as if the reverse reaction was also of first order, and the first-order constant for the rate of approach to equilibrium was determined. This is equal to the sum of the constants for the forward and the back reaction. A knowledge of the position of equilibrium then gave the forward and the backward rate constants. This treatment is open to criticism, since the components present at equilibrium are the *cis*-isomers, and the back reaction has a second-order kinetic form. The results have been recalculated by using, for the value for the optical density at 3000 Å after " infinite time," that calculated for a similar solution containing only the aquoammine isomers, which have very similar extinction coefficients at this wavelength. The semilogarithmic plot then departs from linearity after about 40—50% reaction, but it is easy to measure the initial slope, and from it to calculate the true first-order rate constant for the aquation. These recalculations are reported in Table 2, together with the value obtained in this investigation at 72·8°.

TABLE 2. *Spectrophotometric first-order rate constants for the aquation of trans-*$[Co\ en_2(NH_3)Cl]^{2+}$ *in* 0·1—0·17N-$HClO_4$.

Temperature	89·9°	72·8°	62·6°	62·6°
$10^3 \times$ Initial [Complex] (M)	3·82	2·55	2·42	3·92
$10^5 k_1$ (sec.$^{-1}$)	41·7	8·12	2·88	2·90

(2b) *Steric course.* When this reaction was first studied by Nyholm and Tobe it was thought that the reversibility of the aquation, leading to an accumulation of some *cis*-chloroammine complex, would make impossible an accurate spectrophotometric determination of the isomeric distribution of the aquoammine species. It has since been shown, however, that such pessimism is unjustified, and that, provided the reaction is carried out in the presence of sufficient acid, a full spectrophotometric analysis is possible.

The absorption spectra of *trans*-chloroamminebis(ethylenediamine)cobalt(III) chloride perchlorate and *cis*- and *trans*-aquoamminebis(ethylenediamine)cobalt(III) bromides have already been published.[5] The full spectrophotometric analysis was carried out by determining the changes in the optical density of an aqueous solution of *trans*-chloroamminebis-(ethylenediamine)cobalt(III) chloride perchlorate, 0·10N with respect to perchloric acid, at three wavelengths, 5220, 5070, and 3000 Å.

TABLE 3. *Molar extinction coefficients.*

Wave-length (Å)	*trans*-Chloroammine	*cis*-Aquoammine	*trans*-Aquoammine
5220	47·7	47·7	36·3
5070	43·2	58·6	43·2
3000	312	19	19·7

The relevant molar extinction coefficients are given in Table 3. The way in which these data were used can be illustrated in the following formula:

$$\%trans\text{-}[Co\ en_2(NH_3)H_2O]^{3+} = 100[(D_{5220}/cl) - 47{\cdot}7]/(36{\cdot}3 - 47{\cdot}7)$$

where D_{5220} is the optical density of the solution at 5220 Å, c is the initial concentration of the chloroammine complex, and l is the length of the light path. The percentage of *trans*-$[Co\ en_2(NH_3)Cl]^{2+}$ and of *cis*-$[Co\ en_2(NH_3)H_2O]^{3+}$ can be obtained from analogous formulæ using data at 3000 Å and 5070 Å, respectively.

TABLE 4. *Spectrophotometric analysis of trans-*$[Co\ en_2(NH_3)Cl]Cl.ClO_4$ *during its aquation at* 72·8°.

Initial concn. of *trans*-$[Co\ en_2(NH_3)Cl]^{2+}$ = 0·00255M. Hydrogen-ion concn. = 0·100N.

Time (min.)		0	21·2	40·5	60·0	90·5	124·5	165·0	210·0	268·0
% *trans*-$[(NH_3)Cl]$	calc.	100	90	82	75	64	54	45	36	27
	found	100	92	82	75	65	55	47	39	32
% *trans*-$[(NH_3)H_2O]$	calc.	0	9	16	23	30	37	41	43	43
	found	0	6	15	22	30	38	41	42	38
% (*cis*-$[(NH_3)H_2O]$	calc.	0	0	1	3	5	9	14	21	30
	found	0	0	0	0	4	8	15	20	31

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Table 4 gives the result of the application of these formulæ to an actual run. The composition is given in terms of percentage of total amount of complex ion present. For the first 25% of the reaction, no *cis*-product has been detected. This is a very good indication that no *cis*-product is produced in the actual act of aquation, *i.e.*, that *trans*-[Co $en_2(NH_3)Cl]^{2+}$ gives 100% *trans*-[Co $en_2(NH_3)H_2O]^{3+}$ on reacting with water.

That the *cis*-product is formed only as a result of the rearrangement of the *trans*-aquoamminebis(ethylenediamine)cobalt(III) cation can be seen by comparing the experimental results with those calculated for a reaction of the form

$$\textit{trans}\text{-}[Co\ en_2(NH_3)Cl]^{2+} + H_2O \xrightarrow{k_1} \textit{trans}\text{-}[Co\ en_2(NH_3)H_2O]^{3+} + 8Cl^-$$

$$\textit{trans}\text{-}[Co\ en_2(NH_3)H_2O]^{3+} \xrightarrow{k_2} \textit{cis}\text{-}[Co\ en_2(NH_3)H_2O]^{3+}$$

where $k_1 = 8{\cdot}12 \times 10^{-5}$ sec.$^{-1}$ and $k_2 = 5{\cdot}70 \times 10^{-5}$ sec.$^{-1}$. These values were obtained experimentally by the methods outlined in sections (2*a*) and (1) respectively.

The agreement is good for the first half-life and then deviations appear. These can be directly related to the appearance of *cis*-chloroamminebis(ethylenediamine)cobalt(III) cations, produced by the back reaction. The spectrum of the solution after ten half-lives corresponds very closely to that of a mixture of 87% of *cis*-aquoammine complex and 13% of *cis*-chloroammine complex.

(3) *Aquation of the* trans-*Bromoamminebis(ethylenediamine)cobalt*(III) *Cation.*—(3*a*) *Kinetics.* The rate has been determined spectrophotometrically by following the changes in the optical density at 3000 Å. At this wavelength, the molar extinction coefficient of *trans*-[Co $en_2(NH_3)Br]S_2O_6$ is 960, much greater than the value of about 19 for both of the aquoammine products. It was therefore possible to determine the rate constants of the aquation accurately.

Since the aquation is reversible, it is not possible to follow it to completion. The values used for the optical density of a solution after "infinite time" (D_∞) were those calculated for a solution containing only the aquoammine isomers in the same concentration. The semilogarithmic plots do not depart significantly from linearity during the first two half-lives, so that it is a simple matter to determine the initial slopes.

The rate constants for the reaction, measured at three different temperatures, are given in Table 5.

TABLE 5. *First-order rate constants for the aquation of* *trans*-[Co $en_2(NH_3)Br]^{2+}$ *in* 0·1N-$HClO_4$.

$10^4 \times$ Initial [Complex] (M)	10^5k (sec.$^{-1}$)	$10^4 \times$ Initial [Complex] (M)	10^5k (sec.$^{-1}$)	$10^4 \times$ Initial [Complex] (M)	10^5k (sec.$^{-1}$)
At 72·8°		At 60·0°		At 45·0°	
1·36	37·4	1·36	9·6	1·04	1·57
2·69	38·7	2·69	9·5	2·08	1·63
5·38	37·9	5·38	9·4	5·21	1·64
29·5	38·5	26·9	9·2		

(3*b*) *Steric course.* The increase in the rate of aquation on going from the chloro- to the bromo-complex makes it easier to isolate the aquation from the subsequent rearrangement of the products. However, a consideration of the rate constants of the two reactions will show that the rearrangement will have made considerable progress before the initial aquation is complete.

The absorption spectrum of *trans*-[Co $en_2(NH_3)Br]S_2O_6$ is given in Fig. 1. When this was considered in conjunction with the spectra of the *cis*- and *trans*-products, it was found that an accurate full analysis, like that described in section (2*b*), was not possible. However, the *trans*-bromoammine- and the *trans*-aquoammine-bis(ethylenediamine)-cobalt(III) cations have the same molar extinction coefficients at 5170 Å ($\varepsilon = 38{\cdot}6$), whereas the *cis*-aquoammine complex ion absorbs more strongly ($\varepsilon = 50{\cdot}3$). It was therefore possible to calculate the amount of *cis*-aquoammine cation present at any stage.

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Table 6 shows how ε_{5170} varies with time for a typical run. The amount of *cis*-aquoammine complex ion that is present is also calculated, and it is apparent that no *cis*-product is detected until after the first half-life of the reaction. This result is quite consistent

TABLE 6. *Appearance of* cis-*aquoamminebis(ethylenediamine)cobalt*(III) *cations in an aqueous solution originally containing* trans-*bromoamminebis(ethylenediamine)-cobalt*(III) *dithionate.*

Temperature = 72·8°. Initial concn. of *trans*-[Co $en_2(NH_3)Br]S_2O_6$ = 0·00295M. Solvent = 0·10N-$HClO_4$.

Time (sec.)	0	300	600	900	1380	1980	2765	3600	4530
ε_{5170}	38·4	38·6	38·6	38·4	38·6	38·8	39·0	39·2	40·0
cis-Product (%) ...	0	0	0	0	0	2	3	5	12

(The half-life of the aquation under these conditions is 1800 sec., whereas the half-life of the rearrangement is 12,000 sec.)

with the assumption that the actual act of aquation produces only *trans*-aquoammine cations, and that the *cis*-aquoammine cations appear only as a result of subsequent rearrangement.

(4) *Aquation of* trans-*nitratoamminebis(ethylenediamine)cobalt*(III) *Dithionate.*—(4a) *Kinetics.* The rates of aquation of this complex ion were determined spectrophotometrically at 3000 Å, by the method described previously. At this wavelength the molar

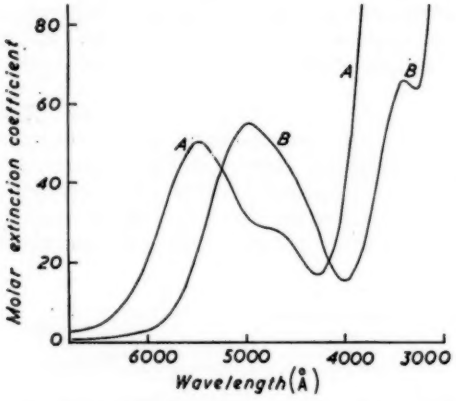

FIG. 1. *Absorption spectra of* (*A*) trans-[Co $en_2(NH_3)Br]S_2O_6$, *and* (*B*) trans-[Co $en_2(NH_3)NO_3]S_2O_6$ *in* 0·1N-*perchloric acid.*

extinction coefficient of the complex is 211. The change in the optical density of a solution in the course of the reaction is therefore much less than that found in the aquation of the corresponding *trans*-bromoammine complex, and thus the kinetics had to be studied at higher complex concentrations, where Beer's law was not strictly obeyed.

The molar extinction coefficient at 3000 Å of a solution of the complex in 0·1N-perchloric acid was found to decrease according to a first-order rate law from 211 for the pure *trans*-nitratoammine complex to 35 after ten half-lives. Thereafter it decreased very slowly to a final value of 20 at a rate corresponding roughly to that of the isomeric rearrangement. The extra absorption (35 rather than 20), first observed in the solution which had reacted substantially to completion, may be due to the presence of small traces of the *trans*-nitroamminebis(ethylenediamine)cobalt(III) complex ($\varepsilon \sim 800$), which then decompose, in the presence of acid, at the rate of the observed slow optical change. These observations, however, are also consistent with the idea that there is some form of interaction between nitrate ions and the *trans*-aquoammine cation, resulting in an increase in the absorption of light in the near-ultraviolet region. Thus pure *trans*-[Co $en_2(NH_3)H_2O](NO_3)_3$ in the millimolar region of concentration has a molar extinction coefficient of 34 at 3000 Å,

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whereas that of the bromide and the perchlorate is 19. This effect was not observed with the *cis*-isomer.

Because of these observations, the first-order rate constants for the aquation were calculated by using the experimentally determined optical density of the solution after ten half-lives had passed, as "D_∞." The first-order rate constants are in Table 7.

TABLE 7. *First-order rate constants for the aquation of trans-*$[Co\ en_2(NH_3)NO_3]^{2+}$ *in* 0·1N-$HClO_4$.

$10^4 \times$ Initial [Complex] (M)	10^4k (sec.$^{-1}$)	$10^4 \times$ Initial [Complex] (M)	10^4k (sec.$^{-1}$)	$10^4 \times$ Initial [Complex] (M)	10^4k (sec.$^{-1}$)
At 60·0°		At 45·0°		At 30·0°	
3·40	6·5	3·83	1·05	9·43	0·142
8·51	6·6	9·43	1·04	13·2	0·141
11·93	6·7	13·4	1·05	19·2	0·141

(4b) *Steric course.* A full spectrophotometric analysis of the reaction mixture was not possible because of the spectra of the three species. {See Fig. 1 for the absorption spectrum of *trans*-$[Co\ en_2(NH_3)NO_3]S_2O_6$.} However, since the aquation is about fifty times faster than the rearrangement, such a treatment is not really necessary.

The absorption spectrum of an aqueous solution of *trans*-$[Co\ en_2(NH_3)NO_3]S_2O_6$ in 0·1N-perchloric acid, which had been kept at 60° for 3 hr (roughly ten half-lives), was found to correspond exactly to that expected for a solution containing aquoamminebis(ethylenediamine)cobalt(III) nitrate in the proportions of 95% of *trans*- to 5% of *cis*-isomer. The amount of *cis*-isomer found corresponded almost exactly to that which would have been formed by the rearrangement in this time.

DISCUSSION

Adamson and Basolo [2] studied the deuterium isotope effect upon the rate of the aquation of the chloro- and bromo-pentamminecobalt(III) cations, and concluded that the transition state corresponds to that expected for a bimolecular reaction with attack from that side of the octahedron which bears the outgoing group. The isotope effect was said to indicate that the reaction process is assisted by hydrogen-bonding between the outgoing ligand, the incoming water, and a *cis*-ammonia ligand (Fig. 2).

Ašperger and Ingold [1] have also discussed the nature of the transition state for bimolecular aquation with special reference to the isomeric $[Co\ en_2(NO_2)Cl]^+$ ions, and have also deduced attack adjacent to the outgoing group. In this case the evidence is very strong, being based on a study of the products of the reaction. The detailed mechanism, however, is quite different from that put forward by Adamson and Basolo. It is suggested that water, by virtue of the electronegativity of the oxygen, can make use of one of the empty 4*d* orbitals of the cobalt atom in order to establish its attack. In the transition state the water and the chlorine are each bound by a 3*d*4*d* hybrid orbital, so that the cobalt atom is making nearly seven full bonds. It is suggested that this process can be achieved most satisfactorily when the water and the chlorine are adjacent in the transition state, thus explaining the retention of configuration.

Our study of the aquation of the complex ions, *trans*-$[Co\ en_2(NH_3)X]^{2+}$, where X = Cl, Br, or NO_3, has shown conclusively that in all three cases aquation is accompanied by complete retention of configuration. This observation is very much in agreement with the mechanism but forward by Ašperger and Ingold, since the nature of the outgoing group would not be expected to influence the steric course of the reaction. If, on the other hand, it were hydrogen-bonding only that brought the incoming group into a position adjacent to the outgoing group, we might expect to find that, when ligands that do not readily form hydrogen bonds are replaced by water, non-adjacent attack is possible.

Examination of the Arrhenius parameters of the three reactions (Table 8) leads us to

believe that Ašperger and Ingold's mechanism is responsible for the attack of water adjacent to the outgoing group, but that when hydrogen-bonding is possible it will lower the activation energy of the process. This is suggested by the circumstance that, along the series Cl, Br, NO_3, the activation energy increases, although the rate increases, and the

TABLE 8. *Parameters of the equation,* $k = B \exp(-E^{\ddagger}/RT)$ *for the reactions* *trans*-$[Co\ en_2(NH_3)X]^{2+} + H_2O = trans$-$[Co\ en_2(NH_3)H_2O]^{3+} + X^-$

X	Cl	Br	NO_3
$E^{\ddagger}$ (kcal./mole)	23·6	24·6	25·5
$\log_{10} B$	10·9	12·0	13·5

free-energy decrement of the aquation, ΔG, as estimated from equilibrium composition, increases. This indicates that breakage of the Co–X bond has not proceeded far in the transition state, but that a stereospecific interaction between the incoming water and the outgoing group, in the order Cl > Br > NO_3 lowers the activation energy, and even more markedly lowers the entropy of activation. This can be understood in terms of hydrogen-

FIG. 2.

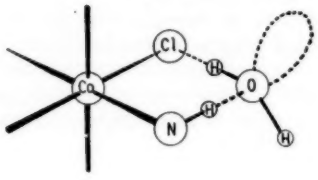
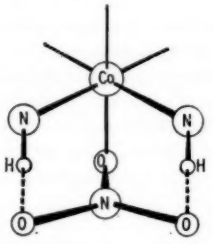


FIG. 3.



bonding, provided that a reasonable suggestion can be made to account for the relative weakness with which the nitrato-group must be assumed to form a hydrogen bond. One possible suggestion is that the two terminal oxygen atoms of the nitrato-group have already taken advantage of their favourable position for hydrogen-bonding with adjacent ammino- or amino-ligands (Fig. 3).

Whether one should assume that incoming water is hydrogen-bonded, not only through its hydrogen to the departing ligand, but also through its oxygen to a hydrogen atom, seems much more doubtful. There seems to be no specific evidence for this process, which retracts the unshared water electrons (Fig. 2) and turns their orbital away from the cobalt nucleus with which they have to combine.

The analogous system, $[Co(NH_3)_5X]^3$, where X = Cl, Br, or NO_3, has been investigated by a number of workers,[6] and the activation energies of the aquation are very similar to those of the acidoamminebis(ethylenediamine)cobalt(III) system. In general, the acidopentamminecobalt(III) cations aquate at rates that are higher than those of the corresponding ethylenediamine complexes. This increased rate has been attributed to the more compact solvent shell about the pentammine complex.[7]

EXPERIMENTAL

Preparations.—*trans*-Chloroamminebis(ethylenediamine)cobalt(III) chloride perchlorate was prepared by the method of Nyholm and Tobe [5] (Found: Co, 16·6%; equiv., 120. Calc. for $C_4H_{19}O_4N_5Cl_3Co$: Co, 16·1%; equiv., 122).

trans-Aquoamminebis(ethylenediamine)cobalt(III) nitrate was prepared by Nyholm and Tobe's method [5] (Found: Co, 14·6. Calc. for $C_4H_{21}O_{10}N_8Co$: Co, 14·7%).

trans-Nitroamminebis(ethylenediamine)cobalt(III) nitrate and bromide, the starting materials

[6] References from Basolo and Pearson, "Mechanisms of Inorganic Reactions," Wiley and Sons, Inc., New York, 1958, p. 122.

[7] Ašperger and Ingold, *J.*, 1956, 2872.

for the following preparations, were prepared by the action of liquid ammonia on *trans*-chloronitrobis(ethylenediamine)cobalt(III) nitrate as described by Werner.[8]

trans-Bromoamminebis(ethylenediamine)cobalt(III) dithionate was prepared by digesting *trans*-nitroamminebis(ethylenediamine)cobalt(III) bromide with bromine-free, hydrobromic acid (40%) on a steam-bath until no more NO_2 was evolved. On evaporation of the mixture to dryness, a mixture of the *cis*- and the *trans*-bromoamminebis(ethylenediamine)cobalt(III) bromide was obtained. It was possible to obtain the *trans*-isomer in a pure form by fractional crystallisation, but this is tedious and results in very small yields. It was found that, if a solution of the mixed bromides was treated with sodium dithionate, the insoluble *trans*-bromoamminebis(ethylenediamine)cobalt(III) dithionate was precipitated first. The dithionate was recrystallised from hot water and obtained as fine pale purple needles (Found: Br, 18·5; Co, 14·0%; equiv., 148. Calc. for $C_4H_{19}O_6N_5S_2BrCo$: Br, 18·3; Co, 14·5%; equiv., 145).

trans-Nitratoamminebis(ethylenediamine)cobalt(III) dithionate was prepared in an analogous way. *trans*-Nitroamminebis(ethylenediamine)cobalt(III) nitrate (24 g.) was added slowly to a hot (85°) 6N-solution of nitric acid (80 ml.), and the mixture was kept at this temperature until the evolution of NO_2 slackened. The solution was then decanted into an evaporating basin, and heated upon a steam-bath until the evolution of NO_2 had almost ceased. It is essential to steer between insufficient reaction, on one hand, when the product will be seriously contaminated with unchanged nitro-complex, and too much reaction, on the other, when low yields are obtained, because the product rearranges to the *cis*-form, and also because dinitrato-complexes are formed.

The very thick syrup was allowed to cool, and was then dissolved in water (60 ml.) at 30°. The solution was filtered, and the filtrate treated with solid sodium dithionate (6 g.). An orange-pink precipitate consisting almost entirely of *cis*-nitratoamminebis(ethylenediamine)-cobalt(III) dithionate came down. The mixture was left for 24 hr., and the product filtered off (11·5 g.). Sufficient solid sodium acetate was added to the filtrate to raise the pH to 5, and then sodium dithionate was added to saturate the solution. Needle-shaped crystals of *trans*-nitratoamminebis(ethylenediamine)cobalt(III) dithionate started to separate. The mixture was left at 0° for 24 hr., and the *trans*-isomer, together with some sodium dithionate, was filtered off, washed with water to remove the sodium dithionate, and recrystallised as quickly as possible from water at 60° (yield 1·5 g). The salt, dried over calcium chloride, is anhydrous (Found: equiv., 140. Calc. for $C_4H_{19}O_9N_6S_2Co$: equiv., 139).

Analytical Procedures.—(a) *Equivalent weight.* About 0·1 g. of the complex was weighed out accurately and suspended, or dissolved, in 10 ml. of water and treated with excess of alkali. The solution containing $[Co\ en_2(NH_3)OH]^{2+}$ was passed through a column of Amberlite IR-120 resin in the acid form. The cationic species were replaced by hydrogen ions, and the effluent was titrated with standard sodium hydroxide. Since the complex ion is retained on the resin in the aquo-form, one mole of the complex will liberate 3 equiv. of acid.

(b) *Halogen determination.* The effluent from the above treatment was also analysed argentometrically for the halogen originally present in the complex.

(c) *Cobalt determination.* About 0·1 g. of the complex was weighed out and dissolved in 20 ml. of N-ammonia solution. The solution was heated to 60° and hydrogen sulphide was passed through it until all the cobalt had been precipitated as its sulphide, which was filtered off and roasted. The cobalt was then estimated iodometrically by Laitinen and Burdett's method.[9]

Methods of Measurement.—Spectrophotometric measurements were made by using a 4 cm. silica cell and a Unicam SP.500 spectrophotometer.

The methods used to make up the solutions for kinetic measurements require mention. *trans*-$[Co\ en_2(NH_3)Cl]Cl.ClO_4$ is quite soluble in water: the reaction solution could thus be made up by adding the appropriate amount of water and perchloric acid to a weighed out amount of complex. *trans*-$[Co\ en_2(NH_3)Br]S_2O_6$ is nearly insoluble in water, and was therefore handled as follows. The appropriate amount of complex (0·1 g.) was weighed into a standard flask, and 1·0 ml. of 72% perchloric acid was added. This caused the salt to dissolve, the dithionate group being destroyed and sulphur dioxide evolved. The flask was evacuated with a water pump in order to remove as much as possible of the sulphur dioxide, and the volume was made up to 100 ml. with distilled water. This solution was then used as a stock solution, and diluted

[8] Werner, *Annalen*, 1912, **386**, 227.
[9] Laitinen and Burdett, *Analyt. Chem.*, 1952, **23**, 1268.

as required. The appropriate amount of 1·00N-perchloric acid was added at this stage, so as to maintain the pH at 1. There was no difference in the absorption spectrum of a solution so prepared and that of a solution of the bromide prepared and purified by another method, less convenient than that here described. The treatment, therefore, had no effect upon the complex ion. *trans*-$[Co\ en_2(NH_3)NO_3]S_2O_6$, although insoluble in water, will dissolve in 0·1N-perchloric acid. The appropriate amount of complex was weighed out, and suspended in 10. ml. of water; then 1 ml. of 72% perchloric acid was added to dissolve the complex. (This is quite a good way of distinguishing the *trans*-isomer from the *cis*-, which remains undissolved after this treatment.)

After the appropriate solution had been made up to volume, aliquot parts of about 11 ml. were sealed into clean, dry, Pyrex test-tubes. These were placed in a thermostat, and individual tubes were withdrawn at intervals and cooled as quickly as possible in ice. The contents were then allowed to warm to room temperature and poured into the spectrophotometer cell for measurement.

Thermostats held the temperatures constant to $\pm 0{\cdot}05°$. Light was excluded, either by using Ucepal baths or, at the lower temperatures, by adding Nigrosine Black to the water in the bath.

The author is indebted to Professor Sir Christopher Ingold, F.R.S., Professor R. S. Nyholm, F.R.S., and Professor D. P. Craig for advice and discussion.

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University College, Gower St., London, W.C.1. [*Received, May 4th,* 1959.]

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764. *Molecular Polarisation and Molecular Interaction. Part VIII.* The Apparent Dipole Moments of Some Derivatives of* N*-Methylaniline in Benzene and Dioxan Solutions.*

By J. W. Smith and (Miss) S. M. Walshaw.

The dipole moments of *p*-bromo-, 2,4-dibromo-, 2,4,6-tribromo-, *p*-nitro-, and 2,4-dinitro-*N*-methylaniline have been determined in benzene and in dioxan. The dipole moments suggest that the mesomeric effect of the methylamino-group is repressed only slightly by one *o*-methyl group and not at all by one *o*-bromine atom. It is sterically hindered strongly, however, by two *o*-methyl groups but is only partially inhibited by two *o*-bromine atoms. These observations support the suggestion that the forces between a hydrogen atom or methyl group and a bromine atom may be less repulsive than those between a hydrogen atom or methyl group and another methyl group. When no steric effects arise the additional moments in dioxan increase with increasing interaction moment. For 2,4-dibromo-, and 2,4,6-tribromo-methylaniline, however, they are lower than for methylaniline itself, this reflecting the steric opposition to complex formation or to the mesomerism of the dioxan complex.

The dipole moments of mesidine and aminodurene in benzene are equal [1] (1·45 D) and slightly lower than the moment of aniline (1·53 D), suggesting that *o*-methyl groups may cause a slight steric repression of the mesomeric effect of the amino-group. On the other hand the moment of 2,4,6-tribromoaniline [2] (1·73 D) is appreciably greater than that of aniline, indicating that there is no repression of mesomerism in this compound. The dipole moments of dimethylmesidine [3] (1·03 D) and 2,4,6-tribromo-*NN*-dimethylaniline [2] (1·02 D), however, are nearly equal and much lower than that of*NN*-dimethylaniline (1·58 D), indicating that there is almost complete repression of the mesomerism in these compounds. It appears, therefore, that *ortho*-substituents prevent the plane of the

* Part VII, *J.*, 1957, 4527.

[1] Smith, *J.*, 1953, 109.
[2] Few and Smith, *J.*, 1949, 2663.
[3] Ingham and Hampson, *J.*, 1939, 981.

dimethylamino-group from coming near to the plane of the aromatic ring, but have no such steric effect, or only a slight one, upon the amino-group. Similar evidence is provided by the ultraviolet absorption spectra and molecular refractions of these compounds.[4]

Further, the apparent dipole moments of primary aromatic amines are appreciably greater in dioxan than in benzene solution. For nuclear-substituted anilines the difference between the observed moment in benzene solution and the value calculated by vector summation of the moments of the substituent groups has been intepreted as an interaction moment μ_{int}, and the difference between the apparent moments in dioxan and benzene solutions as an additional component $\Delta\mu_{vect}$ arising from electron displacements accompanying hydrogen bonding between an amino-hydrogen atom and an oxygen atom of a dioxan molecule.[5] For *para*-monosubstituted and other symmetrically substituted anilines both μ_{int} and $\Delta\mu_{vect}$ were assumed to act along the axis of the N–C bond, whilst for *meta*-monosubstituted and 2,4-disubstituted anilines they were assumed to act along an axis parallel to the line joining $C_{(1)}$ and $C_{(3)}$. For *meta*- and *para*-monosubstituted and 2,4- and 3,5-disubstituted anilines the values of μ_{int} and $\Delta\mu_{vect}$ derived on this basis are related, within experimental error, by the empirical expression $\Delta\mu_{vect} = 0{\cdot}33 + 0{\cdot}255\ \mu_{int}$. For 2,4,6-trisubstituted anilines, however, $\Delta\mu_{vect}$ is lower than would be expected from this relationship, an effect which is attributable to steric inhibition of the mesomeric effect in the complex with dioxan.[6]

It would therefore be expected that the mesomeric effect of the methylamino-group should be, at most, only slightly restricted by the presence of one *ortho*-substituent, since it can attain near coplanarity with the ring when the methyl group is towards the side of the molecule remote from the substituent. On the other hand there might be some steric effect in the dioxan complex. It would be expected, however, that the mesomerism might be inhibited strongly by the presence of two *ortho*-substituents. Evidence in this direction was provided by the observation [1] that the dipole moment of methylmesidine in benzene (1·22 D) is much lower than that of *N*-methylaniline (1·68 D), whilst its moment in dioxan is only slightly higher than that in benzene.

The dipole moments of other derivatives of methylamine have now been measured in benzene and dioxan. The results are summarised in Table 1, which also includes data for methylmesidine and for benzene solutions of *N*-methyl-*o*-toluidine and *N*-methyl-2,4- and -2,6-xylidine.

TABLE 1. *Dipole moments* (D).

	μ_{benz}	μ_{diox}	μ_{calc}	μ_{int}	$\Delta\mu_{vect}$
N-Methylaniline	1·68	1·86	—	—	0·23
N-Methyl-*o*-toluidine	1·76 [7]	—	1·85	−0·08	—
N-Methyl-2,4-xylidine	1·54 [7]	—	1·58	−0·08	—
N-Methyl-2,6-xylidine	1·28 [7]	—	1·98	−0·97	—
N-Methylmesidine	1·22 [1]	1·26 [1]	1·68	−0·72	0·08
p-Bromo-*N*-methylaniline	3·31	3·56	3·04	0·29	0·26
2,4-Dibromo-*N*-methylaniline	2·88	3·10	2·62	0·28	0·23
2,4,6-Tribromo-*N*-methylaniline	1·68	1·81	1·68	0·00	0·17
N-Methyl-*p*-nitroaniline	6·82	7·12	5·41	1·43	0·30
N-Methyl-2,4-dinitroaniline	6·36	6·58	4·74	1·70	0·23

To interpret the dipole moments in terms of μ_{int} and $\Delta\mu_{vect}$, some assumption must be made regarding the axis of the dipole in the *N*-methylaniline molecule. If the mesomeric effect in *N*-methyl-*p*-toluidine is the same as in *N*-methylaniline, it follows from the dipole moments of these molecules in benzene solution (1·41 [7] and 1·68 D,[1] respectively) and the dipole moment of toluene (0·37 D) that the axis of the dipole is inclined at 38½° to the bond linking the nitrogen atom to the ring, the positive end being away from the ring. Similar

[4] Wepster, *Rec. Trav. chim.*, 1957, **76**, 357.
[5] Smith and Walshaw, *J.*, 1957, 3217.
[6] Smith and Walshaw, *J.*, 1957, 4527.

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calculation from the moment of *N*-methyl-*m*-toluidine [7] (1·58 D) leads to an angle of 42°. In the latter case the calculation involves the assumption that if there are any preferred conformations of the methylamino-group, those in which the *N*-methyl group is on the same side of the molecule as the *C*-methyl group have equal probability with the conformations in which the amino-hydrogen atom is on that side of the molecule. Analogous calculations indicate that in aniline and dimethylaniline the dipoles are inclined at 48½° and 34°, respectively, to the bond joining the nitrogen atom to the ring, so an inclination of 40° to this bond in methylaniline seems to be a reasonable assumption.

On this basis " theoretical " moments of the compounds have been calculated from the contributory group moments, which have been taken as 1·56 and 4·01 D, respectively, for a single bromine atom and nitro-group, and as 1·47 and 3·83 D, respectively, for the two bromine atoms and two nitro-groups in the 2,4-disubstituted methylanilines. The results are shown in the third column of Table 1, the fourth and fifth columns of which indicate the values of μ_{int} and $\Delta\mu_{vect}$, which were deduced from the observed and calculated moments by the same method as was used for the derivatives of aniline.[6]

The moments of *N*-methylmesidine and *N*-methyl-2,4-xylidine indicate that two *o*-methyl groups produce a very considerable steric depression of the mesomerism of the methylamino-group. One *o*-methyl group, however, has a much smaller effect, comparable with that suggested by the moments of *o*-toluidine and mesidine. The ultraviolet absorption spectra of both aniline and *N*-methylaniline derivatives suggest that *o*-methyl groups produce no depression of the mesomerism.[4,8] It is possible, therefore, that the decrease in the dipole moments of these compounds as compared with the calculated values may be due to in-plane deflexion of the methyl groups, but such deflexion would have to amount to about 17° to account for the results. It seems more likely, therefore, that the discrepancy is concerned with the fact that the dipole moment depends only on the ground state of the molecule, but the ultraviolet spectrum depends also on the excited state.

The interaction moments of *p*-bromo- and *p*-nitro-*N*-methylaniline are greater than those of the corresponding aniline derivatives (0·20 and 1·08 D, respectively [5]), but less than those of the *NN*-dimethylaniline derivatives (0·37 and 1·48 D, respectively [9]). As in the aniline series the interaction moment for the 2,4-dinitro-compound is greater than that of the *p*-nitro-derivative, so the tendency for intramolecular hydrogen-bond formation seems to encourage, rather than otherwise, the near-coplanarity of the methylamino-group with the plane of the ring. There appears to be little, if any, steric inhibition of mesomerism in 2,4-dibromo-*N*-methylaniline, since for this compound μ_{int} is, within experimental error, the same as for *p*-bromo-*N*-methylaniline.

In benzene solution the dipole moment of 2,4,6-tribromo-*N*-methylaniline is equal to that of methylaniline and much higher than that of methylmesidine. This contrasts with the relative values for the corresponding derivatives of dimethylaniline. The evidence suggests, therefore, that the mesomerism is suppressed strongly in methylmesidine, but is only partly repressed in 2,4,6-tribromo-*N*-methylaniline. This inference becomes reasonable if it is assumed that the molecule cannot assume a conformation with the methyl group near to the bromine atom, but can take up a conformation with the amino-hydrogen atom near to the plane of the benzene ring and in proximity to the bromine atom (Figure, *A*). In such a conformation the orientation of the lone-pair orbital of the nitrogen atom relative to the plane of the ring will not permit so great an orbital overlap with the π-orbitals of the ring as does the most favourable conformation of *N*-methylaniline itself (Figure, *B*), but should furnish an appreciable overlap without bringing the methyl group near to a bromine atom. Hence a diminished, but still substantial mesomeric effect would be expected. Such a conformation would not be possible for 2,4,6-tribromo-*NN*-dimethylaniline, so the dimethylamino-group must be arranged with the

[7] Fischer, *Acta Chem. Scand.*, 1950, **4**, 1197.
[8] Burgers, Hoefnagel, Verkade, Visser, and Wepster, *Rec. Trav. chim.*, 1958, **77**, 491.
[9] Smith, " Steric Effects in Conjugated Systems," Butterworths, London, 1958, p. 141.

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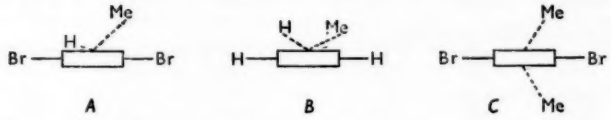
two methyl groups on opposite sides of the plane of the ring and roughly equidistant from it (Figure, *C*), a conformation which precludes appreciable mesomerism between the group and the ring.

It appears that the methylmesidine molecule cannot take up a conformation corresponding with that proposed for 2,4,6-tribromo-*N*-methylaniline. This supports the suggestion made previously that the forces between a hydrogen atom or methyl group and



a bromine atom may not be so repulsive as those between a hydrogen atom or methyl group and another methyl group.

The values of $\Delta\mu_{\text{vect}}$ are all much smaller than for the corresponding aniline derivatives. This may arise either because of a smaller extent of formation of a hydrogen-bonded complex, or because such bonding is attended by a smaller electron displacement. The values parallel the results for aniline derivatives, however, in indicating that when no steric effects arise $\Delta\mu_{\text{vect}}$ increases with increasing μ_{int}. The fact that the values for 2,4-dibromo- and 2,4,6-tribromo-*N*-methylaniline are smaller even than the value for *N*-methylaniline itself reflects the steric opposition to complex formation or to the mesomerism of the dioxan complex. Similar effects were observed with 2,4,6-trisubstituted anilines.[6]

Experimental

Materials.—*p*-Bromo-*N*-methylaniline was prepared by treating *p*-bromoaniline toluene-*p*-sulphonate with dimethyl sulphate. After repeated recrystallisation from aqueous alcohol, the product was hydrolysed with 70% sulphuric acid and the mine separaated by steam distillation. After being dried (CaO) it was distilled *in vacuo*: it had b. p. 135°/12 mm. (lit.[10] 137—138°/14 mm.).

2,4-Dibromomethylaniline was prepared by brominating *N*-methylaniline by Fries's method [10] and recrystallised from alcohol: it had m. p. 48·6° (lit.[10] 48°).

2,4,6-Tribromo-*N*-methylaniline was also made by Fries's method, but it was found necessary to keep the reaction mixture for about three weeks at room temperature to complete the reaction. After being recrystallised from alcohol: it had m. p. 39·5° (lit.[10] 39°).

Commericial, pure *N*-methyl-*p*-nitroaniline was recrystallised repeatedly from aqueous alcohol: it had m. p. 152·2° (lit.[11,12] 151—152°). *N*-Methyl-2,4-dinitroaniline was prepared by Glazer, Hughes, Ingold, James, Jones, and Roberts's method [13] and recrystallised from aqueous acetone: it had m. p. 178·7° (lit.[13] 177—178°).

Benzene and dioxan were purified and dried as described previously.[14]

Methods and Results.—The dielectric constants, specific volumes, and refractive indices of the solutions were determined at 25° by the methods used previously.[6] The results are recorded in Table 2, where $\Delta\varepsilon$, Δv, and Δn indicate the differences between the dielectric constants, specific volumes, and refractive indices, respectively, of the solutions and those of the pure solvents. The calculations from these results are summarised in Table 3, where α, β, and γ indicate the limiting values of $d\varepsilon/dw$, dv/dw, and dn^2/dw, respectively, at zero concentration, and the other symbols have their usual significance. The accurate determination of $[R_D]$ for *N*-methyl-*p*-nitro- and 2,4-dinitro-aniline was precluded by the sparing solubility of these compounds in benzene: the values shown in brackets in Table 3 were obtained by adding the difference between the $[R_D]$ values of methylaniline and aniline to the $[R_D]$ values of *p*-nitro- and 2,4-dinitro-aniline, respectively. Otherwise $P_{2\infty}$ and $[R_D]_2$ were also calculated by the procedures used previously.[14] The values of the dipole moments shown and used in the

[10] Fries, *Annalen*, 1906, **346**, 174.
[11] Blanksma, *Rec. Trav. chim.*, 1902, **21**, 270.
[12] Meldola and Salmon, *J.*, 1888, **53**, 775.
[13] Glazer, Hughes, Ingold, James, Jones, and Roberts, *J.*, 1950, 2674.
[14] Few and Smith, *J.*, 1949, 753.

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TABLE 2. *Polarisation data.*

10^6w	$10^4\Delta\varepsilon$	$-10^5\Delta v$	$10^4\Delta n$
p-Bromo-N-methylaniline in benzene			
11,717	779	563	9
28,019	1882	1347	21
44,473	3000	2137	33
60,471	4135	2907	45
87,383	6037	4201	65
p-Bromo-N-methylaniline in dioxan			
10,717	930	325	11
19,992	1776	605	25
35,156	3118	1066	47
59,635	5357	1805	80
2,4-Dibromo-N-methylaniline in benzene			
9194	341	575	7
19,838	737	1246	15
31,662	1185	1968	24
42,066	1585	2606	32
61,417	2353	3814	47
2,4-Dibromo-N-methylaniline in dioxan			
11,026	529	487	15
22,906	1104	1017	30
32,507	1577	1437	43
42,479	2073	1878	56
53,728	2632	2371	70
2,4,6-Tribromo-N-methylaniline in benzene			
14,239	155	985	10
25,228	275	1742	17
34,904	381	2401	24
48,062	527	3321	32
54,921	608	3789	39
2,4,6-Tribromo-N-methylaniline in dioxan			
12,885	187	664	15
21,475	311	1107	25
29,327	425	1507	34
37,791	548	1944	44
46,525	674	2391	54
57,725	836	2965	67
N-Methyl-p-nitroaniline in benzene			
517	173	17	—
942	317	32	—
1521	511	57	—
2035	680	72	—
2675	893	98	—
3384	1133	121	—
N-Methyl-p-nitroaniline in dioxan			
1786	742	32	5
3359	1406	65	9
5372	2251	99	13
6842	2867	129	18
9486	3970	180	23
12,675	5304	233	31
N-Methyl-2,4-dinitroaniline in benzene			
353	75	15	—
615	133	27	—
1174	256	51	—
1614	363	73	—
2060	463	91	—
N-Methyl-2,4-dinitroaniline in dioxan			
683	181	21	1
1809	498	52	3
2472	655	73	4
3094	861	93	6
4029	1114	123	8

TABLE 3.

N-Methylaniline derivative	Solvent	100α	$-10^3\beta$	$10^3\gamma$	$P_{2\infty}$ (c.c.)	$[R_D]$ (c.c.)	μ (D)
p-Bromo-	Benzene	662	481	223	268·3	44·1	3·31
	Dioxan	871	303	382	303·3	44·4	3·56
2,4-Dibromo-	Benzene	363	621	228	222·5	52·2	2·86
	Dioxan	480	442	371	250·3	53·4	3·10
2,4,6-Tribromo-	Benzene	109	690	206	117·1	59·3	1·68
	Dioxan	145	514	331	127·5	60·5	1·81
p-Nitro-	Benzene	3350	358	—	933·8	[42·4]	6·82
	Dioxan	4185	187	690	1085·7	49·3	7·12
2,4-Dinitro-	Benzene	2250	442	—	865·0	[49·0]	6·36
	Dioxan	2765	300	560	932·6	52·3	6·58

discussion were calculated on the assumption that ${}_\mu P = {}_T P - [R_D]$. The assumption that the distortion polarisation is represented by 1·05 $[R_D]$ leads to values 0·01—0·02 D lower.

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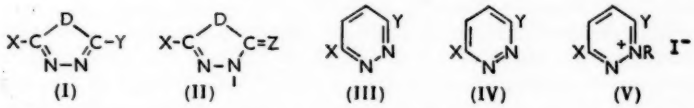
765. *The Structure and Reactivity of Pyridazine Quaternary Salts.**

By G. F. Duffin and J. D. Kendall.

The rate and position of quaternization of a number of substituted pyridazines (III) and dihydropyridazines (VI) and (XI) have been studied and related to the electronic influences of the substituents. The structures of the salts (V) and (XII) so formed have been determined by study of their reactivities, degradation products, and alternative syntheses.

Cyanine dyes have been prepared from those salts containing reactive methyl or methylthio-groups.

In a number of investigations [1] which had as their object the synthesis of cyanine dyes containing new heterocyclic nuclei, the quaternisation of a variety of bases of the general formula (I) or (II) has been studied, where D is the residue of a heterocyclic ring, X and Y are substituents, and Z = O or S. On account of its ease of preparation and aromatic stability, the pyridazine ring appeared very suitable for a more detailed study of the effect of substituents on the rate and position of quaternization. It has been shown [2] that form (III) contributes more to the structure of pyridazine than does form (IV), and pyridazine compounds can be regarded as being of the general formula (I). The majority of the compounds studied contained a methyl or alkylthio-group which may therefore be activated, by suitable quaternization, to take part in the formation of cyanine dyes by reaction with another quaternary salt containing the suitable complementary group.[3]



(I) (II) (III) (IV) (V)

3-Methylpyridazine reacted rapidly with methyl iodide to give a methiodide which must be the salt (V; Y = R = Me, X = H), because treatment with 3-methyl-2-methylthiobenzothiazolium iodide gave a monomethincyanine. 1,6-Dihydropyridazin-6-one was converted into the mercapto-compound by treatment with phosphorus pentasulphide. Methylation then gave 3-methylthiopyridazine (III; X = MeS, Y = H) which reacted fairly slowly with methyl iodide, to give a salt which could not be condensed with 2,3-dimethylbenzothiazolium iodide and must therefore possess the structure (V; X = MeS, Y = H, R = Me). Methyl iodide and 1,6-dihydro-1-methyl-6-thiopyridazine (VI; X = H, Z = S, R = Me), prepared from the corresponding oxo-compound, reacted very rapidly, to give a quaternary salt which, with 2,3-dimethylbenzothiazolium iodide, gave the same dye as was prepared from 3-methylpyridazine methiodide. Further, the salt obtained from the thione (VI) was different from that from 3-methylthiopyridazine and therefore the salt from the thione must be (V; R = Me, X = H, Y = MeS) and the dye can only be (VII; R = Me, X = H). The methyl group (+*I*) is thus seen to activate the adjacent nitrogen atom whereas the alkylthio-group (−*I*) in the same position deactivates it. The inductive effect of the groups therefore appears to be the most important, because the mesomeric effects are of the same sign whereas the inductive effects are of opposite sign.[4]

* Preliminary experiments were reported as part of a paper presented to the Fine Chemicals Group of the Society of Chemical Industry at King's College, London, December, 1954, and the complete paper was read at the XVIth Internat. Congr. Pure Appl. Chem., Paris, July, 1957.

[1] [a] Kendall and Duffin, B.P. 730,489; [b] Kendall, Duffin, and Waddington, B.P. 743,133; [c] *Idem*, B.P. 766,380; [d] Kendall and Duffin, B.P. 775,386; [e] Duffin, Fry, and Kendall, B.P. 785,939.
[2] Maccoll, *J.*, 1946, 671.
[3] Kendall and Suggate, *J.*, 1949, 1503.
[4] Ingold, "Structure and Mechanism in Organic Chemistry," Bell, London, 1953, p. (*a*) 71; (*b*) 77; (*c*) 735.

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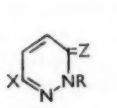
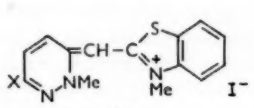
Mizzoni and Spoerri[5] reported, after this investigation had commenced, that 4-methylpyridazine gave 1,4-dimethylpyridazinium iodide and attributed the formation of the latter salt to the mesomeric effect of the methyl group which they believed acted by hyperconjunction.

As was expected, 6-methyl-3-methylthiopyridazine, in which both of the above mentioned groups are operative, gave the salt (V; R = Y = Me, X = MeS). The structure of this salt was shown by its reaction with 3-methyl-2-methylthiobenzothiazolium iodide to give the dye (VII; X = MeS) and also because the salt was different from the salt (V; R = X = Me, Y = MeS) prepared by the very rapid reaction of methyl iodide with 1,6-dihydro-1,3-dimethyl-6-thiopyridazine (VI; R = X = Me, Z = S). The last salt condensed with 2,3-dimethylbenzothiazolium iodide to give the dye (VII; X = Me).


(VI)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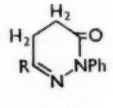
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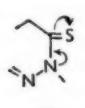

(IX)

3,6-Di(methylthio)pyridazine reacted very slowly with methyl iodide, to give the salt (V; R = Me, X = Y = MeS) from which the dye (VII; X = MeS) was obtained, while 3,6-dimethylpyridazine reacted rapidly, to give the salt (V; R = X = Y = Me) which gave the dye (VII; X = Me); and these dyes prepared from the symmetrical bases were identical with corresponding dyes obtained from the two isomeric salts (V; R = Y = Me, X = MeS) and (V; R = X = Me, Y = MeS).

Two pyridazine quaternary salts have already been described. 3-Chloro-6-methylpyridazine was reported[6] as giving the salt (V; R = Et, Y = Me, X = Cl) as the bromide. The corresponding methiodide has now been prepared and shown to be the salt (V; R = Y = Me, X = Cl) by its reaction with 3-methyl-2-methylthiobenzothiazolium iodide in ethanolic sodium acetate to give the dye (VII; X = Cl). The use of pyridine as the reaction medium gave a deep blue material which could not be purified but was suggestive of the formation of some tricarbocyanine-like substance (cf. the formation of tricarbocyanines from other heterocyclic chloro-compounds in presence of pyridine).[7] Again the $+I$ effect of the methyl group and the $-I$ of the chlorine atom control the quaternization.

Poppenberg[8] treated 3-phenylpyridazine with methyl iodide to obtain a salt of unknown structure. Oxidation of this salt with potassium ferricyanide has given 1,6-dihydro-1-methyl-3-phenylpyridazin-6-one (IV; R = Me, X = Ph, Z = O), which was then prepared unambiguously by the methylation of 1,6-dihydro-3-phenylpyridazin-6-one; the methiodide must therefore be (V; R = Me, X = Ph, Y = H). 6-Methyl-3-phenylpyridazine reacted at moderate speed with methyl iodide to give the salt (V; R = Y = Me, X = Ph), the structure of which was proved by reaction on the methyl group to give the dye (VII; X = Ph). 6-Methylthio-3-phenylpyridazine reacted slowly with methyl iodide, to give a salt containing a reactive methylthio-group and this, in turn, gave a dye identical with that obtained from the 6-methyl analogue, indicating that the latter methiodide was (V; R = Me, Y = MeS, X = Ph). This structure was proved by the formation of the identical product by the very rapid reaction of methyl iodide with 1,6-dihydro-1-methyl-3-phenyl-6-thiopyridazine (VI; R = Me, Z = S, X = Ph), prepared in turn by treatment of the corresponding oxo-compound with phosphorus pentasulphide. It would seem that the combined electronic[4c] and steric effects of the phenyl group more than offset the $-I$ effect of the methylthio-group.

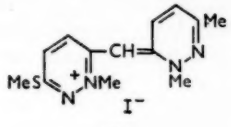
[5] Mizzone and Spoerri, *J. Amer. Chem. Soc.*, 1955, **76**, 2201.
[6] Halverson and Hirst, *J. Chem. Phys.*, 1951, **19**, 711.
[7a] Kendall, B.P. 424,264; [b] Ficken and Kendall, personal communication.
[8a] Poppenberg, *Ber.*, 1901, **34**, 3262; [b] Knorr, *Annalen*, 1886, **236**, 137.

1,4,5,6-Tetrahydro-3-methyl-1-phenyl- and -1,3-diphenyl-pyridazin-6-one (VIII; R = Me or Ph) were treated with phosphorus pentasulphide, but, even under the mildest conditions used, the extra hydrogen atoms were lost from the 4- and the 5-position and the corresponding 1,6-dihydro-6-thiopyridazines were formed. These compounds, in common with all the thiones (VI; Z = S), reacted very rapidly with methyl iodide, to give the quaternary salts (V; R = Ph, Y = MeS, X = Me or Ph) which contained reactive methylthio-groups and with 2,3-dimethylbenzothiazolium iodide gave cyanine dyes. The very high reactivity of the thiones is presumably due to mesomeric shift (IX) which possesses the additional driving force of making the ring truly aromatic.

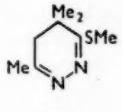
3-Methoxy-6-methylpyridazine reacted at moderate speed with methyl iodide, to give the salt (V; R = Y = Me, X = MeO) which contained a reactive methyl group and yielded cyanine dyes. 3-Methoxy-6-methylthiopyridazine reacted very slowly with methyl iodide and gave a salt which contained a reactive methylthio-group and so gave a cyanine dye; this proved identical with the corresponding dye obtained from 3-methoxy-1,6-dimethylpyridazinium iodide. The former salt must therefore be 3-methoxy-1-methyl-6-methylthiopyridazinium iodide (V; R = Me, X = MeO, Y = MeS). Once again, the methoxy-group, possessing a stronger $-I$ effect than the methylthio-group,[4a] results in quaternization on the N-atom remote from the methoxy in spite of the higher $+M$ effect of that group.[4b] The very strong influence of the methoxy-group to inhibit quaternization was finally shown by the very slow formation of the salt (V; R = Me, Y = Ph, X = MeO) from 3-methoxy-6-phenylpyridazine and methyl iodide. The structure of this product was assigned on the evidence of its failure to give 1,6-dihydro-1-methyl-3-phenylpyridazin-6-one when the salt was boiled with pyridine; this product would have been expected [8] to be formed from the isomeric material (V; R = Me, Y = MeO, X = Ph).

The dihydro-oxopyridazines (VI; Z = O) could not be brought into reaction with methyl iodide or methyl toluene-*p*-sulphonate even under drastic conditions. Fusion of 2-methylthiobenzothiazole, methyl toluene-*p*-sulphonate, and 1,6-dihydro-3-methylpyridazin-6-one gave the cyanine (VII; X = MeO), showing that O-methylation takes place under these conditions.

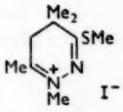
Although in no case could two methiodides be isolated from the same base, the " joint fusion " method [9] of preparing monomethincyanine dyes gave evidence that under these conditions 6-methyl-3-methylthiopyridazine yielded some of the isomeric salt (V; R = X = Me, Y = MeS). Thus fusion of that base with methyl toluene-*p*-sulphonate gave an orange melt which after being boiled with pyridine gave some of the dye (X) which must be formed by reaction between the toluene-*p*-sulphonates of the salts (V; R = Y = Me,



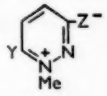
(X)



(XI)



(XII)



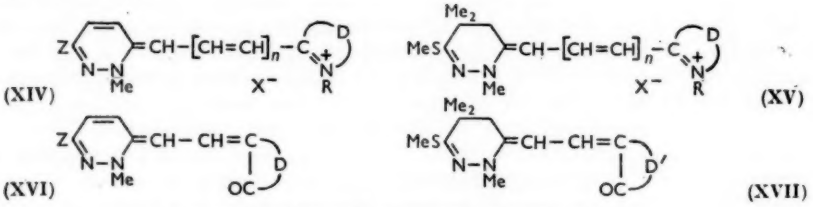
(XIII)

X = MeS) and (V; R = X = Me, Y = MeS) and was indeed formed by the reaction between the two isolated salts. 6-Methyl-3-methylthiopyridazine, 2-methylbenzothiazole, and methyl toluene-*p*-sulphonate similarly gave 5% of the dye (VII; X = Me). Although all attempts to obtain 4,5-dihydropyridazines free from substituents in the 4- and the 5-position were unsuccessful, the *gem*-dimethyl derivative (XI) was obtained. This compound behaved in a similar manner to 6-methyl-3-methylthiopyridazine, giving the salt (XII), which contained a reactive methyl group, and dyes were prepared by reaction on that group.[1d]

All the quaternary salts (V; Y = MeS) were readily converted into thiones (VI; Z = S)

[9] Kendall, B.P. 438,420.

by treatment with boiling pyridine [10] or aqueous sodium sulphide,[11] and it was therefore of interest to see if those containing a methylthio- or methoxy-substituent in the *other* position relative to the nitrogen would give such compounds which could only be dipolar, *i.e.*, (XIII; Z = O or S). The action of boiling pyridine on these salts (V; X = MeS or MeO) gave very discoloured materials, but cold aqueous sodium sulphide rapidly gave a high yield of a white precipitate from the salts (V; X = MeS, Y = H; X = MeS, Y = Me; and X = MeO, Y = Me). The products, which all melted below 100° with decomposition, were insoluble in water and, though moderately soluble in most organic solvents, could not be crystallized: they analysed correctly for the salts minus MeI, but molecular-weight determination showed association. They decomposed in a few days and did not regenerate the salts (V; X = MeS or MeO) on treatment with methyl iodide, giving impure orange, cyanine-like materials. It seems unlikely therefore that these substances possess the structure (XIII).* It is noteworthy that the compound from the methoxy-salt contained no sulphur, indicating that the sodium sulphide was not attacking the ring. The action of sodium sulphide upon the methiodide of 3-methoxy-6-phenylpyridazine gave a product which, although it was not stable enough for analysis, resembled in properties the materials from the 6-methyl analogues and provides some support for the structure (V; X = MeO, R = Me, Y = Ph).



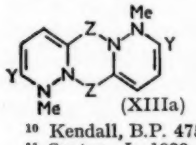
(XIV) (XV) (XVI) (XVII)

D = residue of five- or six-membered heterocyclic nucleus.

In addition to the monomethincyanines obtained in the elucidation of the structures of the salts, other monomethincyanines (XIV and XV; $n = 0$), trimethincyanines (XIV and XV; $n = 1$), and dimethinmerocyanines (XVI) and (XVII) were prepared from the salts (V; Y = Me) and (XII) by the usual methods. All the pyridazine monomethincyanines possess two widely spaced, rather broad maxima; *e.g.*, the dye (VII; R = X = Me) has maxima at 371 (ε 19,200) and 437 mμ (ε 22,100); those from the dihydro-*gem*-dimethylpyridazines show a single maximum of higher extinction coefficient, *e.g.*, (4,5-dihydro-1,4,4-trimethyl-3-methylthio-6-pyridazine)(3-methyl-2-benzothiazole)monomethincyanine has a maximum at 426 mμ (ε 50,100). The trimethincyanines, of both types, all show a single maximum of characteristic high extinction coefficient.

Experimental

3-Mercapto-6-methylpyridazine.—In spite of the statement by Gregory *et al.*,[12] the action of phosphorus pentasulphide on 1,6-dihydro-3-methylpyridazin-6-one was found to be the best method of preparing this mercapto-compound. The freshly dried pyridazinone [13] (132 g.), phosphorus pentasulphide (268 g.), and xylene (300 ml.) were stirred and heated under reflux



(XIIIa)

* The authors are grateful for the suggestion by a referee that the formula (XIIIa) might represent these compounds. It is considered likely that some combination of this type, perhaps containing the residues from two or more molecules of quaternary salts, might explain the behaviour of these materials, but on the information at present available no final decision is possible.

[10] Kendall, B.P. 475,647.
[11] Sexton, *J.*, 1939, 470.
[12] Gregory, Overend, and Wiggins, *J.*, 1948, 2199.
[13] Overend and Wiggins, *J.*, 1947, 239.

for 3 hr. The xylene was then removed by evaporation and the residue decomposed with hot water (3 l.). After cooling, the precipitated solid was filtered off and the filtrate extracted with chloroform (4 × 400 ml.). The residue obtained by evaporation of the chloroform was combined with the first solid and recrystallized from ethanol, to give the mercapto-compound as deep yellow rhombic crystals, m. p. 203° (96 g., 64%).

3-Methyl-6-methylthiopyridazine.—3-Mercapto-6-methylpyridazine (56 g.) was dissolved in N-sodium hydroxide (444 ml.) and shaken with methyl iodide (28 ml.) for 1 hr. The resulting solution was extracted with chloroform (3 × 100 ml.) and the extracts were evaporated. The residue was distilled to give the *methylthio-compound* as a pale yellow oil, b. p. 135—141°/20 mm. (44 g., 70%) (Found: C, 51·15; H, 5·6. $C_6H_8N_2S$ requires C, 51·3; H, 5·7%).

1,6-Dihydro-3-methyl-1-phenyl-6-thiopyridazine.—1,4,5,6-Tetrahydro-3-methyl-1-phenylpyridazin-6-one [14] (9·4 g.) was dissolved in hot toluene (100 ml.), phosphorus pentasulphide (11 g.) was added, and the mixture boiled under reflux for 1 hr. The toluene was decanted while still hot and the residue extracted with boiling toluene (2 × 250 ml.). Evaporation of the combined toluene solutions gave a yellow oil which, when kept with ethanol, solidified. Recrystallization from ethanol gave the *thione* as yellow plates, m. p. 109° (6·1 g., 59%) (Found: N, 13·6; S, 15·9 $C_{11}H_{10}ON_2S$ requires N, 13·8; S, 15·8%).

3-Mercaptopyridazine.—1,6-Dihydropyridazin-6-one [15] (13·5 g.), pyridine (80 ml.), and phosphorus pentasulphide (12 g.) were boiled under reflux for 1 hr. Water (400 ml.) was added and the pyridine removed by evaporation. The resulting solid was filtered from the cooled residue and recrystallized from ethanol, to give the *thiol* as yellow needles, m. p. 170° (8·0 g., 51%) (Found: S, 28·6. $C_4H_4N_2S$ requires S, 28·5%).

3-Methylthiopyridazine was obtained from the mercapto-compound in the manner described for the 6-methyl analogue, and distilled to give a pale yellow solid, b. p. 138°/15 mm., m. p. 37—38° (65%) (Found: S, 25·5. $C_5H_6N_2S$ requires S, 25·4%).

1,6-Dihydro-1-methylpyridazin-6-one.—1,6-Dihydropyridazin-6-one (13·5 g.) was added to a solution from sodium (3·24 g.) in methanol (80 ml.), and methyl iodide (8·8 ml.) was then added. After refluxing for 1 hr., the solution was evaporated from a steam-bath, and the residue extracted with benzene (4 × 50 ml.). Evaporation of the benzene gave an oil which was distilled, to give the colourless *methyl compound*, m. p. 35°, b. p. 110°/15 mm. (8·7 g., 56%) (Found: C, 54·6; H, 5·3. $C_5H_6ON_2$ requires C, 54·4; H, 5·4%).

1,6-Dihydro-1-methyl-6-thiopyridazine.—1,6-Dihydro-1-methylpyridazin-6-one (3·7 g.), xylene (107 ml.), and phosphorus pentasulphide (7·4 g.) were boiled under reflux for 2 hr. After cooling, the tarry solid was filtered off and the filtrate evaporated to give a solid which recrystallized from cyclohexane to give the *thione* as yellow leaflets, m. p. 110° (1·75 g., 41%) (Found: S, 25·7. $C_5H_6N_2S$ requires S, 25·4%).

3-Phenylpyridazine.—3-Mercapto-6-phenylpyridazine (10 g.), water (50 ml.), aqueous ammonia (*d* 0·920; 10 ml.), and Raney nickel paste (40 g., prepared by Brown's method [16]) were heated on a steam-bath for 15 min. and then boiled under reflux for 1½ hr. The mixture was filtered hot and the filtrate cooled to give the product as colourless leaflets, m. p. 98° (cf. Poppenberg [8]) (4·1 g., 49%).

1,6-Dihydro-1-methyl-3-phenylpyridazin-6-one.—Sodium (1·15 g.) was dissolved in methanol (50 ml.), and 1,6-dihydro-3-phenylpyridazin-6-one [17] (8·6 g.) and methyl iodide (3·2 ml.) were added. After boiling under reflux for 2 hr., the solution was diluted with water and cooled, to precipitate the solid *product* which recrystallized from water as colourless needles, m. p. 116° (7·9 g., 85%) (Found: C, 70·75; H, 5·25. $C_{11}H_{10}ON_2$ requires C, 71·0; H, 5·4%).

1,6-Dihydro-1-methyl-3-phenyl-6-thiopyridazine.—1,6-Dihydro-1-methyl-3-phenylpyridazin-6-one (6·2 g.), xylene (40 ml.), and phosphorus pentasulphide (7·4 g.) were boiled under reflux for 2 hr. The xylene was decanted while still hot and, on cooling, gave the solid *thione* which was filtered off and recrystallized from ethanol as yellow needles, m. p. 151° (4·7 g., 70%) (Found: N, 13·6; S, 15·9. $C_{11}H_{10}N_2S$ requires N, 13·8; S, 15·9%).

3-Chloro-6-methylthiopyridazine.—Hydrogen sulphide was passed into a solution of sodium sulphide nonahydrate (55·3 g.) in water (175 ml.) until 8·4 g. had been absorbed. 3,6-Dichloropyridazine [18] (38 g.) was added, and the mixture shaken and set aside for 1 hr. Ethanol (175 ml.)

[14] Fischer, *Annalen*, 1886, **236**, 147.
[15] Homer, Gregory, Overend, and Wiggins, *J.*, 1948, 2195.
[16] Brown, *J. Soc. Chem. Ind.*, 1950, **69**, 355.
[17] Gabriel and Colman, *Ber.*, 1899, **32**, 399.
[18] Mizzoni and Spoerri, *J. Amer. Chem. Soc.*, 1951, **73**, 1873.

was then added and the solution boiled under reflux for 1 hr. On cooling to 0° overnight, a solid was precipitated which was filtered off. The filtrate was acidified with concentrated hydrochloric acid (40 ml.), giving the crude mercapto-compound which was filtered off and dried in the air for 2 hr. (28·4 g.).[19] The mercapto-compound, in N-sodium hydroxide (201 ml.), was shaken with methyl iodide (11·4 g.) for 1 hr. The resulting solid was filtered off and recrystallized from light petroleum (b. p. 100—120°) to give *3-chloro-6-methylthiopyridazine* as colourless needles, m. p. 103—104° (12·2 g., 30%) (Found: C, 37·6; H, 3·6; S, 20·0; Cl, 22·25. $C_5H_5N_2SCl$ requires C, 37·2; H, 3·1; S, 19·95; Cl, 22·15%).

3-Methoxy-6-methylthiopyridazine.—3-Chloro-6-methylthiopyridazine (15·0 g.) was added to a solution from sodium (2·16 g.) in methanol (66 ml.), and the whole was boiled under reflux for 2 hr. The methanol was then removed under reduced pressure, and water (100 ml.) added to the residue, to give the solid *methoxy-compound* which recrystallized from water as colourless needles, m. p. 87° (8·8 g., 60%) (Found: C, 45·9; H, 5·5; S, 20·6. $C_6H_8ON_2S$ requires C, 46·2; H, 5·3; S, 20·5%).

1,6-Dihydro-1,3-dimethyl-6-thiopyridazine.—1,6-Dihydro-1,3-dimethylpyridazin-6-one [20] (3·9 g.), xylene (100 ml.), and phosphorus pentasulphide (6·9 g.) were boiled under reflux for 2 hr., the mixture was cooled, and the liquid decanted. Evaporation of the xylene left a yellow oil which was distilled (b. p. 115—119°/0·8 mm.), to give the *thione* as a yellow solid, m. p. 91—93° (2·6 g., 59%). Recrystallization from ethanol gave yellow leaflets, m. p. 100° (Found: S, 22·75. $C_6H_8N_2S$ requires S, 22·8%).

1,6-Dihydro-1,3-diphenyl-6-thiopyridazine.—1,4,5,6-Tetrahydro-1,3-diphenylpyridazin-6-one [21] (12 g.), phosphorus pentasulphide (10·7 g.), and toluene (100 ml.) were boiled under reflux for 90 min. The resulting yellow solution was decanted from some tarry solid and evaporated under a vacuum, to leave a yellow solid *thione* which recrystallized from ethanol as bright yellow needles, m. p. 158—159° (7·2 g., 56%) (Found: C, 72·9; H, 5·0. $C_{16}H_{12}N_2S$ requires C, 72·9; H, 4·6%).

1,6-Dimethyl-3-methylthiopyridazinium Iodide.—3-Methyl-6-methylthiopyridazine (10 g.), dry benzene (20 ml.), and methyl iodide (10 ml.) were boiled under reflux. Some solid was deposited after 5 min. and at the end of 2 hr. the precipitated solid was filtered off and washed well with dry acetone and dried *in vacuo*, to give the yellow *salt*, m. p. 123° (18·2 g., 88%). Recrystallization from ethanol gave yellow needles, m. p. 132—134° (Found: C, 30·0; H, 4·1; S, 11·3. $C_7H_{11}N_2SI$ requires C, 29·75; H, 3·9; S, 11·35%).

The following quaternary salts were prepared by similar methods, reaction times are in parentheses: the salts formed yellow needles from ethanol unless otherwise stated:

1,6-Dihydro-1,3-dimethyl-6-thiopyridazine gave (¼ hr.) *1,3-dimethyl-6-methylthiopyridazinium iodide* (87%), m. p. 159° (Found: C, 29·5; H, 4·2; S, 11·4; I, 44·7. $C_7H_{11}N_2SI$ requires C, 29·75; H, 3·9; S, 11·35; I, 45·0%); 3-methylpyridazine [8] gave (1 hr.) *1,6-dimethylpyridazinium iodide* (75%) (from acetone), m. p. 80° (Found: I, 53·4. $C_6H_9N_2I$ requires I, 53·8%); 3-methyl-6-phenylpyridazine [22] gave (1½ hr.) *1,6-dimethyl-3-phenylpyridazinium iodide* (34%), m. p. 197° (Found: C, 46·25; H, 4·4; I, 39·7. $C_{12}H_{13}N_2I$ requires C, 46·2; H, 4·15; I, 40·8%); 3-phenylpyridazine gave (1 hr.) *1-methyl-3-phenylpyridazinium iodide* (79%), m. p. 174° (cf. ref. 8); 3-methylthio-6-phenylpyridazine gave (2 hr.) *1-methyl-6-methylthio-3-phenylpyridazinium iodide* (49%), m. p. 177° (Found: C, 41·7; H, 4·0. $C_{12}H_{13}N_2SI$ requires C, 41·8; H, 3·8%), the identical salt (m. p. and mixed m. p.) being obtained (¼ hr., 91%) from methyl iodide and 1,6-dihydro-1-methyl-3-phenyl-6-thiopyridazine; 3-methylthiopyridazine gave (1 hr.) *1-methyl-3-methylthiopyridazinium iodide*, m. p. 147—148° (77%) (Found: C, 26·95; H, 3·5; S, 12·0. $C_6H_9N_2SI$ requires C, 26·9; H, 3·35; S, 11·95%); 1,6-dihydro-1-methyl-6-thiopyridazine gave (5 min.) *1-methyl-6-methylthiopyridazinium iodide*, m. p. 188° (79%) (Found: C, 26·7; H, 3·4. $C_6H_9N_2SI$ requires C, 26·9; H, 3·35%); 1,6-dihydro-3-methyl-1-phenyl-6-thiopyridazine gave (15 min.) *3-methyl-6-methylthio-1-phenylpyridazinium iodide*, m. p. 197—198° (73%) (Found: C, 41·9; H, 3·95. $C_{12}H_{13}N_2SI$ requires C, 41·8; H, 3·8%); 3-methoxy-6-methylpyridazine gave (2 hr.) *1,6-dimethyl-3-methoxypyridazinium iodide*, needles, m. p. 160° (92%) (Found: C, 31·7; H, 4·5. $C_7H_{11}ON_2I$ requires C, 31·6; H, 4·15%); 3,6-di(methylthio)pyridazine [19] gave (2 hr.) *1-methyl-3,6-di(methylthio)pyridazinium iodide* (from acetone), m. p. 160—162°

[19] Cf. Druey, Meier, and Eichenberger, *Helv. Chem. Acta*, 1954, **37**, 121.
[20] Homer, Gregory, and Wiggins, *J.*, 1948, 2192.
[21] Pulvermacher, *Ber.*, 1893, **26**, 462.
[22] Paal and Dencks, *Ber.*, 1903, **36**, 492.

(59%) (Found: S, 20·3. $C_7H_{11}N_2S_2I$ requires S, 20·4%); 3-6-dimethylpyridazine [23] gave (30 min.) 1,3,6-*trimethylpyridazinium iodide* (from acetone), m. p. 110—111° (93%) (Found: I, 50·4. $C_7H_{11}N_2I$ requires I, 50·75%); 3-methoxy-6-methylthiopyridazine gave (4 hr.) 3-*methoxy*-1-*methyl*-6-*methylthiopyridazinium iodide*, m. p. 198° (51%) (Found: C, 27·8; H, 3·9; S, 11·0. $C_7H_{11}ON_2SI$ requires C, 28·2; H, 3·7; S, 10·7%); 1,6-dihydro-1,3-diphenyl-6-thiopyridazine gave (15 min.) 6-*methylthio*-1,3-*diphenylpyridazinium iodide*, m. p. 183° (45%) (Found: C, 49·9; H, 3·75; S, 8·15. $C_{17}H_{15}N_2SI$ requires C, 50·3; H, 3·7; S, 7·9%); 3-methoxy-6-phenylpyridazine [17] gave (4 hr.) 3-*methoxy*-1-*methyl*-6-*phenylpyridazinium iodide* (from ethyl acetate–ethanol), colourless needles, m. p. 153—154° (41%) (Found: C, 43·5; H, 4·0. $C_{12}H_{13}ON_2I$ requires C, 43·8; H, 3·95%); and 3-chloro-6-methylpyridazine [8] gave (1 hr.) 3-*chloro*-1,6-*dimethylpyridazinium iodide*, a yellow solid, m. p. 185° (68%), which could not be recrystallized (Found: N, 10·1. $C_6H_8N_2ClI$ requires N, 10·3%).

Oxidation of 1-*Methyl*-3-*phenylpyridazinium Iodide*.—The salt (1·5 g.) was dissolved in warm water (36 ml.) and added slowly with stirring to a solution of potassium ferricyanide (3·9 g.) and potassium hydroxide (1·3 g.) in water (35 ml.) at 5°. A solid was deposited fairly quickly. The temperature was allowed to rise to 10°. After 30 minutes' stirring, the mixture was warmed to 40° for a few minutes, cooled, and filtered, to give 1,6-dihydro-1-methyl-3-phenylpyridazin-6-one as buff needles, m. p. 114—115°, mixed m. p. with the authentic material 115—116° (0·67 g., 72%).

Action of Bases on 1-*Methyl*-6-*methylthio*-3-*phenylpyridazinium Iodide*.—(*a*) The methiodide (4·0 g.) and pyridine (20 ml.) were boiled under reflux for 2 hr. and diluted with water (150 ml.). The resulting solid was filtered off and recrystallized from ethanol, to give 1,6-dihydro-1-methyl-3-phenyl-6-thiopyridazine as yellow needles, m. p. 151° (0·95 g., 46%), identical with the material obtained as above. (*b*) The methiodide (2·0 g.) was dissolved in water (100 ml.), and sodium sulphide monohydrate (2·0 g.) in water (10 ml.) added. The mixture was left overnight and the resulting solid filtered off and recrystallized, to give the thione (0·42 g., 44%).

Preparation of Monomethincyanines.—(*a*) 3-Ethyl-2-methylbenzothiazolium iodide (0·76 g.), 1-methyl-6-methylthio-3-phenylpyridazinium iodide (0·81 g.), and ethanol (12 ml.) were boiled under reflux until all the solid had dissolved. Triethylamine (0·5 ml.) was added, giving an immediate orange-yellow colour, and, after a few minutes, solid began to be precipitated. After boiling for 10 min., the mixture was cooled, and the solid filtered off and recrystallized from methanol to give (1-*methyl*-3-*phenyl*-6-*pyridazine*)(3-*ethyl*-2-*benzothiazole*)*monomethincyanine iodide* (dye no. 1) as orange-red needles, m. p. 260° (0·43 g., 46%) (Found: C, 53·1; H, 4·4. $C_{21}H_{20}N_3SI$ requires C, 53·2; H, 4·25%).

The monomethincyanines in Table 1 were prepared by similar methods from the intermediates listed. The identity of the bracketed pairs provides evidence for the structures of the pyridazine salts from which the dyes are derived.

(*b*) 3-Methyl-6-methylthiopyridazine (0·75 g.), 2-methylthiobenzothiazole (0·9 g.), and methyl toluene-*p*-sulphonate (1·9 g.) were fused at 130° for 2 hr. Pyridine (10 ml.) was added and the mixture boiled under reflux for 1 hr., giving an orange solution which was poured into 4% aqueous sodium iodide (50 ml.). The resulting solid was filtered off and recrystallized from methanol, to give (1-methyl-3-methylthio-6-pyridazine)(3-methyl-2-benzothiazole)monomethincyanine iodide (dye no. 4′) as orange-red needles, m. p. 267° (0·92 g., 43%), identical with dye 4 of Table 1.

Similar experiments are summarized in Table 2.

(1,3-*Diphenyl*-6-*pyridazine*)(3-*ethyl*-2-*benzothiazole*)*monomethincyanine Iodide*.—1,3-Diphenyl-6-methylthiopyridazinium iodide (0·82 g.), 3-ethyl-2-methylbenzothiazolium iodide (0·61 g.), anhydrous sodium acetate (0·5 g.), and ethanol (20 ml.) were boiled under reflux for 1 hr., giving a deep orange solution. Pouring the mixture into water precipitated a solid which was filtered off and recrystallized from ethanol, to give the *dye* (no. 11) as red needles with a blue reflex, m. p. 248° (0·5 g., 47%) (Found: S, 6·15; I, 23·4. $C_{26}H_{23}N_2SI$ requires S, 6·0; I, 23·8%).

By a similar process, 3-chloro-1,6-dimethylpyridazinium iodide and 3-methyl-2-methylthiobenzothiazolium iodide gave (3-*chloro*-1-*methyl*-6-*pyridazine*)(3-*methyl*-2-*benzothiazole*)*monomethincyanine iodide* (dye no. 12) from methanol as orange needles, m. p. 254° (31%) (Found: S, 8·00. $C_{14}H_{13}N_3SClI$ requires S, 7·7%), but reaction between the same two salts in pyridine, in the manner used in the experiments of Table 1 gave only a deep blue tar.

[23] Overberger, Byrd, and Mesrobian, *J. Amer. Chem. Soc.*, 1956, **78**, 1962.

Trimethincyanines.—The following exemplifies the procedure: 3-methoxy-1,6-dimethylpyridazinium iodide (0·51 g.) and 2,2′-acetanilidovinyl-1,3,3-trimethylindoleninium iodide (0·89 g.) were dissolved in hot ethanol (10 ml.), and triethylamine (0·5 ml.) was added. After boiling for 1 hr., the solution was added to 3% aqueous sodium iodide (50 ml.) to precipitate a

TABLE 1. *Monomethincyanines* (XIV; $n = 0$).

Dye no.	Pyridazine salt (V; R = Me) X	Y	Other intermediate	Dye (XIV; * $n = 0$) X	R	Yield (%)	M. p.	Found (%) S	Formula	Reqd. (%) S
2	H	Me	A	H	Me	73	265° [a]	8·5	$C_{14}H_{14}N_2SI$	8·35
2′	,,	MeS	B		,,	81		8·45		
3	Me	Me	A	Me	,,	75	289 [a]	7·9	$C_{15}H_{16}N_2SI$	8·05
3′	,,	MeS	B		,,	58		8·1		
4	MeS	,,	B	MeS	,,	90	267 [b]	14·7	$C_{15}H_{16}N_2S_2I$	14·9
4′	,,	Me	A		,,	50		15·0		
5	MeO	MeS	B	MeO	,,	23	232 [a]	7·6	$C_{15}H_{16}ON_2SI$	7·7
5′	,,	Me	A		,,	52		7·7		
6	Ph	,,	A	Ph	,,	84	278 [b]	7·2	$C_{20}H_{18}N_2SI$	7·0
6′	,,	MeS	B		,,	70		6·9		
7	MeO	,,	C	MeO	Et	21	225 [a]	[c]		

* D = 2-benzothiazole residue.

[a] Orange needles from methanol. [b] Red needles from methanol. [c] Found: C, 44·65; H, 5·05 $C_{16}H_{18}ON_2SI$ requires C, 44·8; H, 4·2%.

A = 3-Methyl-2-methylthiobenzothiazolium iodide. B = 2,3-Dimethylbenzothiazolium iodide. C = 3-Ethyl-2-methylbenzothiazolium iodide.

TABLE 2. *Dyes prepared by "joint-fusion."*

Dye no.	Pyridazine	Other intermediate	Dye (XIV; * $n = 0$) Z	X	Yield (%)	M. p.	Found (%)	Formula	Required (%)
8 †	VI; X = R = Me, Z = S	A	Me	Br	46	286°	S, 8·85	$C_{15}H_{16}N_2SBr$	S, 9·15
8′	III; X = Me, Y = MeS		,,	,,	3	,,	S, 9·2		
9	III; X = Ph, Y = Me	B		,,	58	257	S, 7·8; Br, 18·9	$C_{20}H_{18}N_2SBr$	S, 7·8 Br, 19·4
2′	III; X = H, Y = Me	B	H	I	29	267	Identical with no. 2 of Table 1		
10	III; X = OH, Y = Me	B	MeO	Br	19	202	S, 8·65; Br, 21·25	$C_{15}H_{16}ON_2SBr$	S, 8·6 Br, 21·4
10′	III; X = OMe, Y = Me	B	,,	,,	26	,,	S, 8·45; Br, 21·3		

* D = 2-benzothiazole residue. A = 2-Methylbenzothiazole. B = 2-Methylthiobenzothiazole. All the dyes crystallized as orange needles from methanol. † This dye is the bromide of dye no. 3 of Table 1; light-absorption data (Table 4) support this identity.

solid which was filtered off and recrystallized from ethanol; this gave the *dye* (no. 13) as purple needles, m. p. 173—174° (Found: C, 53·7; H, 5·5; I, 27·8. $C_{20}H_{24}ON_2I$ requires C, 53·5; H, 5·35; I, 28·3%).

Other dyes prepared by similar methods are given in Table 3.

Self-condensation of Quaternized 3-Methyl-6-methylthiopyridazine.—The pyridazine (0·75 g.) and methyl toluene-*p*-sulphonate (1·00 g.) were fused as 180° for 5 min. The resulting orange melt was boiled in pyridine (5 ml.) for 1 hr., and poured into 5% aqueous potassium bromide to give an orange solid which recrystallized from methanol to give (*1,3-dimethyl-6-pyridazine*)(*1-methyl-3-methylthio-6-pyridazine*)*monomethincyanine bromide* (dye no. 20) as orange needles, m. p. 247° (decomp.) (0·14 g., 14%) (Found: C, 45·7; H, 5·1. $C_{13}H_{17}N_4SBr$ requires C, 45·8; H, 5·0%). The dye was identical with the product obtained by the following unambiguous method: 3-Methyl-6-methylthiopyridazine (0·35 g.) and 1,6-dihydro-1,3-dimethyl-6-thiopyridazine (0·35 g.) were each fused separately with methyl toluene-*p*-sulphonate (0·5 g.) at 120—130° for 1 hr. Each of the melts was dissolved in pyridine (2·5 ml.), and the solutions

TABLE 3. *Trimethincyanines.*

Dye no.	Pyridazine salt (V; R = Me) X	Y	Other intermediate	Dye (XIV; $n = 1$)	Yield (%)	M. p.	Found (%)	Formula	Reqd. (%)
14	MeS	Me	A	Z = MeS, R = Et, X = I, D = benzoxazole	40	250° [a]	S, 7·4	$C_{18}H_{20}N_3OSI$	S, 7·1
15	,,	,,	B	Z = MeS, R = Et, X = I, D = benzothiazole	72	238 [a]	S, 13·8	$C_{18}H_{20}N_3S_2I$	S, 13·6
16	,,	,,	C	Z = MeS, R = Me, X = I, D = 3,3-dimethylindolenine	54	191 [b]	S, 6·8	$C_{20}H_{24}N_2SI$	S, 6·9
17	,,	,,	D	Z = MeS, R = Me, X = I, D = quinoline-2	58	267 [b]	C, 49·9 H, 4·1	$C_{19}H_{20}N_2SI$	C, 50·8 H, 4·4
18	MeO	,,	A	Z = MeO, R = Et, X = ClO_4, D = benzoxazole	27	232 [c]		$C_{18}H_{20}O_6N_2Cl$	
19	,,	,,	B	Z = Me, R = Et, X = I, D = benzothiazole		197 [d]	C, 47·3 H, 4·5	$C_{18}H_{20}ON_2SI$	C, 47·7 H, 4·4

A = 2-2′-Acetanilidovinyl-3-ethylbenzoxazolium iodide. B = 2-2′-Acetanilidovinyl-3-ethylbenzothiazolium iodide. C = 2-2′-Acetanilidovinyl-1,3,3-trimethylindolenium iodide. D = 2-2′-Ethylthiovinyl-1-methylquinolinium iodide.

[a] Blue needles from methanol. [b] Green needles from methanol. [c] Purple needles from methanol. [d] Purple needles from ethanol.

were mixed and boiled for 15 min. Pouring the resulting orange solution into aqueous potassium bromide precipitated a solid, which on recrystallization from methanol gave the dye as orange needles, m. p. 247° (0·57 g., 68%).

1,4,5,6-*Tetrahydro*-3,5,5-*trimethyl*-6-*oxopyridazine*.—Mesitonic acid (the crude oily product prepared by Lapworth's method [24] was satisfactory and the difficulty accessible pure acid gave no better yield) (14 g.), hydrazine sulphate (14 g.), and 10% aqueous sodium hydroxide (86·5 ml.) were boiled under reflux for 1 hr. and evaporated to leave a white solid. This solid was extracted with hot ethanol (2 × 100 ml.), and the combined extracts were evaporated to an oil which was heated to 180° for 10 min. On cooling, the oil solidified and recrystallized from cyclohexane to give the *pyridazinone* as colourless needles, m. p. 110° (6·5 g., 47%) (Found: C, 60·15; H, 8·9. $C_7H_{12}ON_2$ requires C, 60·0; H, 8·7%).

4,5-*Dihydro*-3-*mercapto*-4,4,6-*trimethylpyridazine*.—The above pyridazinone (29·5 g.), dry xylene (295 ml.), and phosphorus pentasulphide (19 g.) were boiled under reflux for 2 hr. The hot xylene was decanted and the solid residue extracted with boiling benzene (200 ml.). The combined benzene extracts were evaporated to an oil which rapidly solidified. This material was purified by dissolution in N-sodium hydroxide and reprecipitation with hydrochloric acid, dried, and recrystallized from cyclohexane to give the pure *mercapto-compound* as pale yellow needles, m. p. 92° (18·9 g., 59%) (Found: S, 20·5. $C_7H_{12}N_2S$ requires S, 20·5%). This mercapto-compound was methylated, by the method described above for the other compounds, to give 4,5-*dihydro*-4,4,6-*trimethyl*-3-*methylthiopyridazine* as a yellow oil, b. p. 100—105°/0·7 mm. (68%) (Found: C, 56·3; H, 8·5. $C_8H_{14}N_2S$ requires C, 56·4; H, 8·25%), and this in turn gave 4,5-*dihydro*-1,4,4,6-*tetramethyl*-3-*methylthiopyridazinium iodide* as yellow needles (from ethanol), m. p. 213—214° (decomp.) (86%) (Found: C, 35·05; H, 5·55. $C_9H_{17}N_2SI$ requires C, 34·7; H, 5·45%).

(3-*Methyl*-2-*benzothiazole*)(4,5-*dihydro*-1,4,4-*trimethyl*-3-*methylthio*-6-*pyridazine*)*monomethincyanine Iodide*.—4,5-Dihydro-4,4,6-trimethyl-3-methylthiopyridazine (0·27 g.), 2-methylthiobenzothiazole (0·29 g.), and methyl toluene-*p*-sulphonate (0·60 g.) were fused for 90 min. at 130—140°. Pyridine (4·0 ml.) were added and the mixture boiled under reflux for 30 min. to give a yellow solution. Pouring this into aqueous potassium iodide precipitated a solid which was filtered off and recrystallized from methanol, to give the *dye* (no. 21) as orange leaflets, m. p. 266° (0·49 g., 56%) (Found: C, 44·6; H, 5·0. $C_{17}H_{22}N_3S_2I$ requires C, 44·45; H, 4·8%).

The following cyanines were prepared from the dihydropyridazine salt (XII) by the method used for the dyes of Table 3: 2-2′-acetanilidovinyl-3-ethylbenzoxazolium iodide gave dye no. 22 (3-*ethyl*-2-*benzoxazole*)(4,5-*dihydro*-1,4,4-*trimethyl*-3-*methylthio*-6-*pyridazine*)*trimethincyanine iodide*, purple plates (from ethanol), m. p. 251° (12%) (Found: S, 6·75. $C_{20}H_{26}ON_3SI$ requires

[24] Lapworth, *J.*, 1904, **85**, 1219.

S, 6·65%); 2-2′-acetanilidovinyl-3-ethylbenzothiazolium iodide gave dye no. 23 (*3-ethyl-2-benzothiazole*)(*4,5-dihydro-1,4,4-trimethyl-3-methylthio-6-pyridazine*)*trimethincyanine iodide*, purple plates (from methanol), m. p. 259° (10%) (Found: S, 13·0. $C_{20}H_{26}N_3S_2I$ requires S, 12·8%); 2-2-acetanilidovinyl-1,3,3-trimethylindolenium iodide gave dye no. 24 (*1,3,3-trimethyl-2-indolenine*)(*4,5-dihydro-1,4,4-trimethyl-3-methylthio-6-pyridazine*)*trimethincyanine iodide*, blue rhombs (from ethanol, m. p. 254° (32%) (Found: S, 6·5. $C_{22}H_{30}N_3SI$ requires S, 6·45%); and 3-ethyl-2-ethylthiobenzothiazolium iodide gave dye no. 25 (*3-ethyl-2-benzothiazole*)(*4,5-dihydro-1,4,4-trimethyl-3-methylthio-6-pyridazine*)*monomethincyanine iodide*, orange-yellow needles (from ethanol, m. p. 258° (8%) (Found: S, 13·5. $C_{15}H_{24}N_3S_2I$ requires S, 13·5%).

4-(*1,6-Dihydro-1-methyl-3-methylthio-6-pyridazinylidene-ethylidene*)-2-*phenyl-5-oxazolone*.—1,6-Dimethyl-3-methylthiopyridazinium iodide (1·5 g.), 4-ethoxymethylene-2-phenyl-5-oxazolone (1·09 g.), and pyridine (10 ml.) were boiled under reflux for 45 min. The resulting red solution was poured into water, precipitating a solid which was filtered off and recrystallized from methanol to give the pure *dye* (no. 26) as blue needles, m. p. 235—237° (0·4 g., 25%) (Found: S, 9·95. $C_{17}H_{15}N_3O_2S$ requires S, 9·85%).

By a similar process, 5-ethoxymethylene-3-ethyl-2-thiothiazolid-4-one gave 3-*ethyl*-4-(*1,6-dihydro-1-methyl-3-methylthio-6-pyridazinylidene-ethylidene*)-2-*thiothiazolid-4-one* (no. 27) which crystallized from ethanol in purple needles, m. p. 216—218° (78%) (Found: S, 29·4. $C_{13}H_{15}ON_3S_3$ requires S, 29·5%).

By similar processes, reaction of 4,5-dihydro-1,4,4,6-tetramethyl-3-methylthiopyridazinium iodide with 4-ethoxymethylene-4-phenyl-5-oxazolone gave 4-(*1,4,5,6-tetrahydro-1,4,4-trimethyl-3-methylthio-6-pyridazinylidene-ethylidene*)-2-*phenyl-5-oxazolone* (dye no. 28), red needles (from ethanol), m. p. 194° (39%) (Found: C, 64·2; H, 6·15; S, 9·0. $C_{19}H_{21}O_2N_3S$ requires C, 64·5; H, 5·95; S, 9·0%), and with 4-ethoxymethylene-3-ethyl-2-thiothiazolid-4-one gave a dye (no. 29), the 3-*ethyl*-2-*thiothiazolid*-4-*one analogue*, red needles (from ethanol), m. p. 194° (69%) (Found: C, 50·6; H, 6·0. $C_{15}H_{21}ON_3S_3$ requires C, 50·8; H, 5·9%).

TABLE 4. *Light-absorption of the dyes.*

These were determined in ethanol using a Unicam S.P. 500 spectrophotometer.

Dye no.	$\lambda_{max.}$ (mμ)	$10^{-4}E$	Dye no.	$\lambda_{max.}$ (mμ)	$10^{-4}E$	Dye no.	$\lambda_{max.}$ (mμ)	$10^{-4}E$
2	377, 435	2·13, 2·16	8′	371, 437	2·25, 2·70	23	552	11·7
2′	377, 435	2·13, 2·17	15	554	10·7	24	547	11·3
3	371, 438	2·24, 2·71	16	539	9·2	30	553, 570	6·82, 6·82
5	361, 450	2·08, 2·81	21	428	6·85	31	545	9·99
8	371, 437	2·25, 2·69	22	515	10·8			

Bis-(*1-methyl-3-methylthio-6-pyridazine*)*trimethincyanine Iodide*.—1,6-Dimethyl-3-methylthiopyridazinium iodide (1·8 g.), ethyl orthoformate (2·0 ml.), and pyridine (10 ml.) were boiled under reflux for 1 hr. The resulting purple solution was poured into 4% aqueous sodium iodide, precipitating a solid which was filtered off and recrystallized to give the pure *dye* (no. 30) as green leaflets, m. p. 268—269° (0·61 g., 28%) (Found: C, 40·1; H, 4·4. $C_{15}H_{19}N_4S_2I$ requires C, 40·1; H, 4·25%).

By a similar process, the dihydro-salt (XII) gave dye no. 31, *bis*-(*4,5-dihydro-1,4,4-trimethyl-3-methylthio-6-pyridazine*)*trimethincyanine iodide*, purple needles (from methanol), m. p. 282° (24%) (Found: C, 45·0; H, 6·1; S, 12·25. $C_{19}H_{27}N_4S_2I$ requires C, 45·1; H, 6·15; S, 12·6%).

Action of Sodium Sulphide on 1,6-Dimethyl-3-methylthiopyridazinium Iodide.—Sodium sulphide nonahydrate (5·0 g.) in water (25 ml.) was added to the iodide (2·82 g.) in water (25 ml.) at 20°. A solid was precipitated immediately and, after 5 min., was filtered off and washed with water, giving a material of unknown structure as a colourless solid, m. p. 60—62° (1·15 g., 82%) [Found: C, 51·3; H, 6·5; S, 23·0. $(C_6H_8N_2S)_n$ requires C, 51·4; H, 5·7; S, 22·9%]. A solution (1%) in boiling benzene gave no immediate elevation of the b. p. but after about 20 sec. the initially colourless solution became slowly brown and the elevation indicated M ~620. Similarly, 3-methoxy-1,6-dimethylpyridazinium iodide gave a colourless product, m. p. 94—96° (77%) [Found: C, 59·1; H, 6·8; S, 0. $(C_6H_9ON_2)_n$ requires C, 59·0; H, 6·6%]; M (in benzene) similar behaviour as above, ~600]. 1-Methyl-3-methylthiopyridazinium iodide gave a colourless product, m. p. 59—61° (81%) [Found: C, 47·35; H, 4·85. $(C_5H_6N_2S)_n$ requires C, 47·6; H, 4·75%]; M (as before in benzene) ~520]. 3-Methoxy-1-methyl-6-phenylpyridazinium iodide gave a similar product (73%) which decomposed rapidly.

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All these materials became orange on storage or more rapidly on warming, and could not be recrystallized.

Similar treatment of 1-methyl-6-methylthiopyridazinium iodide gave 1,6-dihydro-1-methyl-6-thiopyridazine, m. p. and mixed m. p. 110° (68%); 1,3-dimethyl-6-methylthiopyridazinium iodide gave 1,6-dihydro-1,3-dimethyl-6-thiopyridazine, m. p. and mixed m. p. 100° (53%); 3-methoxy-1-methyl-6-methylthiopyridazinium iodide gave *1,6-dihydro-3-methoxy-1-methyl-6-thiopyridazine*, yellow needles (from cyclohexane), m. p. 107° (67%) (Found: C, 46·0; H, 5·2. $C_6H_8ON_2S$ requires C, 46·2; H, 5·1%).

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766. *The Structure and Reactivity of Triazole Quaternary Salts.*

By G. F. DUFFIN, J. D. KENDALL, and H. R. J. WADDINGTON.

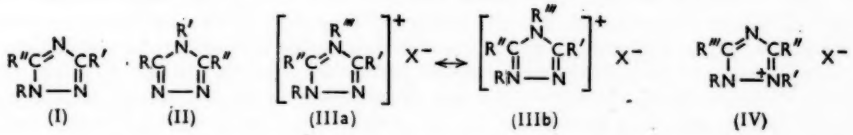
Quaternisation of some 1,3,5-trisubstituted and 1,3-disubstituted 1,2,4-triazoles is shown to take place at the $N_{(4)}$ atom to give salts of the general formula (III). Cyanine and merocyanine dyes are prepared from these salts, as well as from salts of various 3,4,5-trisubstituted 1,2,4-triazoles.

Some 1,2,4-triazolethiones (V, VI, and VII) have been prepared and their structures discussed.

Analysis of the absorption maxima of the dyes prepared indicates that the 1,2,4-triazole nucleus is strongly basic.

FEW triazole quaternary salts have been described; some do not have structures assigned to them,[1] and structures were proposed for others without supporting evidence.[2]

Atkinson and Polya [3] claimed that alkaline degradation of the methiodide of 1,3,5-trimethyl-1,2,4-triazole (I; R = R′ = R″ = Me) gave 1,2-dimethylhydrazine and con-



(I) (II) (IIIa) (IIIb) (IV)

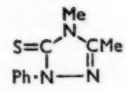
cluded that quaternization had taken place at the $N_{(2)}$ atom to give the salt (IV; R = R′ = R″ = R‴ = Me, X = I). The present authors reported [4] that this degradation gave methylamine and methylhydrazine, and that the methiodides of 1,3,5- (I; R = R′ = R″ = Me) and 3,4,5-trimethyl-1,2,4-triazole (II; R = R′ = R″ = Me) were identical (m. p. and mixed m. p. and infrared absorption), thus proving that quaternisation had taken place at the $N_{(4)}$ atom to give the quaternary salt (III; R = R′ = R″ = R‴ = Me, X = I). In addition, a number of 1,2,4-triazoles have been studied and without exception quaternisation has been found to take place at the $N_{(4)}$ atom to give salts of the general structure (III).

Alkaline degradation of the methiodide of 3,5-dimethyl-1-phenyl-1,2,4-triazole (I; R = Ph, R′ = R″ = Me) gave methylamine and phenylhydrazine,[4] products which could be expected from the structure (III; R = Ph, R′ = R″ = R‴ = Me, X = I). It was also

[1] Andreocci, *Atti R. Accad. Lincei*, 1890, **6**, II, 212; 1897, **6**, I, 294; Gabel and Schmidegg, *Monatsh.*, 1926, **47**, 748; Hernler, *ibid.*, 1927, **48**, 402.
[2] Engelhardt, *J. prakt. Chem.*, 1896, **54**, 153.
[3] Atkinson and Polya, *Chem. and Ind.*, 1954, 462.
[4] Duffin, Kendall, and Waddington, *ibid.*, 1954, 1458.

XUM

found that reaction [5] of the methotoluene-*p*-sulphonate of 3,5-dimethyl-1-phenyl-1,2,4-triazole (I; R = Ph, R′ = R″ = Me) with 3-methyl-2-methylthiobenzothiazolium toluene-*p*-sulphonate gave the same cyanine dye (XI; D = residue of a benzothiazole nucleus, R = Ph, R′ = R″ = R‴ = Me, *m* = 0, X = I) as was formed in reaction between the methotoluene-*p*-sulphonate of 3-methyl-5-methylthio-1-phenyl-1,2,4-triazole (I; R = Ph, R′ = Me, R″ = MeS) and 2,3-dimethylbenzothiazolium toluene-*p*-sulphonate. Since, as described below, 3-methyl-5-methylthio-1-phenyl-1,2,4-triazole (I; R = Ph, R′ = Me, R″ = MeS) was shown to quaternise at the $N_{(4)}$ atom, with both methyl toluene-*p*-sulphonate and methyl iodide, it follows that 3,5-dimethyl-1-phenyl-1,2,4-triazole (I; R = Ph, R′ = R″ = Me) quaternises at the $N_{(4)}$ atom. Quaternary salts of 3-methyl-1-phenyl-1,2,4-triazole (I; R = Ph, R′ = Me, R″ = H) did not give rise to cyanine dyes and thus were assumed to have the structure (III; R = Ph, R′ = R‴ = Me, R″ = H). Neither the methiodide nor the methotoluene-*p*-sulphonate of 3-methyl-5-methylthio-1-phenyl-1,2,4-triazole (I; R = Ph, R′ = Me, R″ = MeS) showed any sign of having a reactive methyl group. On the other hand, both quaternary salts gave the cyanine dye (XI; D = residue of a benzothiazole nucleus, R = Ph, R′ = R″ = R‴ = Me, *m* = 0, X = I), when treated with the corresponding quaternary salts of 2-methylbenzothiazole. Further, the methiodide and boiling pyridine gave a product $C_{10}H_{11}N_3S$ which was shown to be 4,5-dihydro-3,4-dimethyl-1-phenyl-1,2,4-triazole-5-thione (V) since it was also obtained by acetylation of 4-methyl-2-phenylthiosemicarbazide (VIII; R = Me, R′ = Ph, R″ = H) followed by ring closure with sodium ethoxide. The thione (V) rapidly reverted to the methiodide (III; R = Ph, R′ = R‴ = Me, R″ = MeS, X = I) when warmed with methyl iodide. Methylation of 3-mercapto-5-methyl-1-phenyl-1,2,4-triazole [6] (I; R = Ph, R′ = SH, R″ = Me) gave 5-methyl-3-methylthio-1-phenyl-1,2,4-triazole (I; R = Ph, R′ = MeS, R″ = Me) which was also prepared by condensing phenylhydrazine and methyl *N*-acetyldithiocarbamate. The identity of the two products was shown by conversion into identical cyanine dyes. Quaternisation of this base proceeded readily, and both the methiodide and methotoluene-*p*-sulphonate could be used to prepare the same cyanine dyes by reaction of the 5-methyl group, but no reactive methylthio-group was detectable; quaternisation at the $N_{(4)}$ atom therefore was indicated. Dequaternisation of this methiodide (III; R = Ph, R″ = R‴ = Me, R′ = MeS, X = I) with boiling pyridine gave a compound isomeric with with the thione (V) but with a much higher melting point. This new substance was identical (m. p. and mixed m. p. and ultraviolet absorption) with the product obtained by treating 4-methyl-1-phenylthiosemicarbazide (VIII; R = Me, R″ = Ph, R′ = H) with boiling acetic anhydride and is therefore anhydro-3-mercapto-4,5-dimethyl-1-phenyl-1,2,4-triazolium hydroxide (VI; R = Ph, R′ = R″ = Me). The compound (VI) reacted readily with methyl iodide to give the methiodide (III; R = Ph, R″ = R‴ = Me, R′ = MeS, X = I) again. 3-Ethylthio-5-methyl-1-phenyl-1,2,4-triazole (I; R = Ph, R′ = EtS, R″ = Me), prepared from ethyl *N*-acetyldithiocarbamate and phenylhydrazine, also contained a reactive methyl group and formed cyanine dyes. It was of interest to prepare a member of the third type of thione, *e.g.*, (VII). 1-Methyl-2-phenylhydrazine was treated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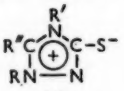
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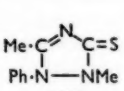
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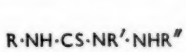
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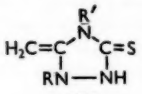

(IX)

in acid solution with potassium thiocyanate, to give 2-methyl-1-phenylthiosemicarbazide (VIII; R′ = Me, R″ = Ph, R = H). This product could be 2-phenyl-1-methylthiosemicarbazide (VIII; R′ = Ph, R″ = Me, R = H); but this appears unlikely because phenylhydrazine gives 1-phenylthiosemicarbazide [7] (VIII; R = R′ = H and R″ = Ph) and

[5] Kendall, B.P. 424,559/1933, 438,420/1934.
[6] Wheeler and Beardsley, *Amer. Chem. J.*, 1902, **27**, 267.
[7] Fischer and Besthorn, *Annalen*, 1882, **212**, 325.

methylhydrazine gives 2-methylthiosemicarbazide [8] (VIII; R = R″ = H, R′ = Me). Acetylation of 2-methyl-1-phenylthiosemicarbazide (VIII; R′ = Me, R″ = Ph, R = H) and ring closure with sodium ethoxide gave 2,3-dihydro-2,5-dimethyl-1-phenyl-1,2,4-triazole-3-thione (VII) which reacted with methyl iodide to give 3-methylthio-2,5-dimethyl-1-phenyl-1,2,4-triazolium iodide (IV; R′ = R‴ = Me, R″ = MeS, R = Ph, X = I).

Whereas the thiones (V and VII) can be represented by a classical covalent structure, anhydro-3-mercapto-4,5-dimethyl-1-phenyl-1,2,4-triazolium hydroxide (VI; R = Ph, R′ = R″ = Me) must be considered as a mesoionic compound.[9] The difference between the three types of thione is illustrated by considering their absorption maxima. Whereas the mesoionic type (VI) absorbs with a maximum in the region of 2400—2500 Å, the other two (V and VII) do so in the region of 2900 Å.

The acylation and ring closure of substituted thiosemicarbazides (VIII; R′ or R″ = H) could give rise to thiadiazole derivatives, a possibility considered by Pulvermacher,[10] Freund,[11] and McKee.[12] However, the ease with which the thiones described in this paper are formed from, and converted into, triazole quaternary salts strongly indicates that they are in fact triazole derivatives. A second mesoionic thione, anhydro-3-mercapto-4-methyl-1-phenyl-1,2,4-triazolium hydroxide (VI; R = Ph, R′ = Me, R″ = H) was formed by dequaternising 3-methylthio-1-phenyl-1,2,4-triazole methiodide (III; R = Ph, R′ = MeS, R″ = H, R‴ = Me, X = I) or by treating 4-methyl-1-phenylthiosemicarbazide (VIII; R = Me, R″ = Ph, R′ = H) with formic acid, and readily reverted to the methiodide (III; R = Ph, R′ = MeS, R″ = H, R‴ = Me, X = I). The similarity between this thione and anhydro-3-mercapto-4,5-dimethyl-1-phenyl-1,2,4-triazolium hydroxide (VI; R = Ph, R′ = R″ = Me) shows that the latter cannot possess the structure (IX; R = Ph, R′ = Me) similar to that suggested by McKee [12] for the diphenyl analogue (IX; R = R′ = Ph). It is clear that both thiones are best represented by the general formula (VI).

In analogy with the work of Freund,[11] 4-methyl-,[10] 4-ethyl-,[13] and 4-phenyl-thiosemicarbazides [10] (VIII; R′ = R″ = H, R = Me, Et, and Ph respectively) were acetylated and cyclised to give the corresponding triazoles (II; R = SH, R″ = Me, R′ = Me, Et, or Ph). Alkylation of these triazoles gave the 4-alkyl(or -phenyl)-5-alkylthio-3-methyl-1,2,4-triazoles (II; R = alkylthio, R″ = Me, R′ = Me, Et, or Ph) in good yield. All these bases were quaternised and converted into cyanine dyes by reaction of the 3-methyl group. Dequaternisation of the methiodide of 3,4-dimethyl-5-methylthio-1,2,4-triazole (II; R′ = R″ = Me, R = MeS) gave rise to a third mesoionic thione (VI; R = R′ = R″ = Me), the properties and absorption spectrum being very similar to those described earlier. These triazoles had quaternised, therefore, at the $N_{(2)}$ atom, *i.e.*, adjacent to the methyl group. This was to be expected by analogy with the quaternisation of certain pyridazine derivatives carried out by two of us.

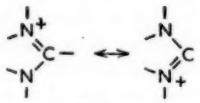
Lastly, cyanine dyes were prepared from the methiodides of a number of 4-aryl-3,5-dimethyl-1,2,4-triazoles (II; R = R″ = Me, R′ = aryl). These methiodides of course must all have the general structure (III; R = R′ = R″ = Me, R‴ = aryl, X = I).

Atkinson and Polya [14] quote values (personal communication from Brown and Bassett) for the electron densities of the unsubstituted triazole molecule which give to the $N_{(4)}$ atom a higher value than to the other two N atoms. Therefore, quaternisation at the 4-position was understandable and, further, as a result of the experiments carried out, it is apparent that the $N_{(4)}$ atom retains the greater share of electron density irrespective of the influence of substituents present in the rest of the molecule. This is well illustrated by the fact that

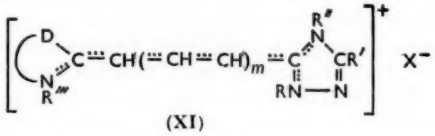
[8] Rodd, " Chemistry of Carbon Compounds," Elsevier, London, 1951, Vol. I, p. 929.
[9] Baker and Ollis, *Quart. Rev.*, 1957, **11**, 15.
[10] Pulvermacher, *Ber.*, 1894, **27**, 622.
[11] Freund, *Ber.*, 1896, **29**, 2483.
[12] McKee, *J.*, 1915, 1136.
[13] Freund and Schwarz, *Ber.*, 1896, **29**, 2486.
[14] Atkinson and Polya, *J.*, 1954, 3319.

3-methyl-5-methylthio- (I; R = Ph, R′ = Me, R″ = MeS) and 3-methylthio-5-methyl-1-phenyl-1,2,4-triazole (I; R = Ph, R′ = MeS, R″ = Me) both quaternise at the $N_{(4)}$ atom. Thus, while interchanging the 3- and the 5-substituent might alter the actual values of the electron densities, the relative values remain unaltered and the $N_{(4)}$ atom retains the greater share. On the other hand, the effect that the substituents had on the electron densities was illustrated when all attempts to quaternise 3,5-dimethylthio-1-phenyl-1,2,4-triazole (I; R = Ph, R′ = R″ = MeS) met with failure owing to the reduction in basicity (*i.e.*, electron density) of the triazole nucleus by the two methylthio-groups.

All the triazole quaternary salts containing a 5-methyl substituent were used to prepare cyanine dyes by classical methods.[15] It was not possible to classify the 1,2,4-triazole nucleus according to Brooker's table of deviations,[16] since it proved impossible to prepare symmetrical cyanine dyes from 1,2,4-triazole quaternary salts. It was also necessary to use pyridine and triethylamine before the dyes could be formed, and this in itself indicated a general lack of reactivity of the quaternary salts which indicates, in Brooker's view,[17] that the parent base is a strong one and, when incorporated in a cyanine dye containing a weakly basic nucleus at the opposite end of the methine chain, would give a large deviation.[16]



(X)



(XI)

Cyanine dyes with a 1,2,4-triazole or a benzimidazole nucleus contain the grouping (X) and it might be expected that, since the benzimidazole nucleus acts as a strongly basic entity, the 1,2,4-triazole nucleus would behave similarly. For example, a trimethincyanine containing a 1,2,4-triazole nucleus and a weakly basic benzoxazole nucleus has three canonical forms. One form contains the positive charge on the benzoxazole nucleus and the other two contain the positive charge on the 1,2,4-triazole nucleus, the stronger basicity of the latter would result in electronic asymmetry of the dye. A measure of this asymmetry in a series of dyes of the general formula (XI; D = residue of a benzoxazole nucleus, R‴ = Et) was obtained by applying Brooker's "sensitivity rule"[18] when considering the absorption maxima of this series. Six dyes of this type were prepared (dyes nos. 1—6 in the experimental section) and their absorption maxima were measured. It was at once apparent that the absorption maxima were highly sensitive to changes in the nature and position of the substituents in the 1,2,4-triazole nucleus. The dyes thus had a high degree of electronic asymmetry. For example, replacement of a 4-methyl group by a 4-phenyl group, *i.e.*, conversion of dye (1) into (3) or of dye (2) into (5), results in a bathochromic shift of about 430 Å. This can be explained by assuming that the 1,2,4-triazole nucleus, being the more basic, retains the larger share of the positive charge in the cation but when phenyl replaces methyl this basicity is reduced and the dye becomes more degenerate, resulting in a bathochromic shift. The shift in going from dye (2) to (5) is slightly less than that in going from dye (1) to (3), presumably because the 3-methylthio-group present in dye (2) reduces the basicity of the triazole nucleus, making the dye rather more symmetrical than the dye (1). Consequently any change has slightly less effect on the absorption maximum than the corresponding change applied to dye (1). Similar chemical changes at the $N_{(1)}$ atom, *i.e.*, dye (1) to (4), or dye (2) to (6), result in somewhat larger bathochromic shifts. Once again, when a 3-methylthio-group is present the shift is smaller. If the degree of electronic asymmetry of dye (1) is assumed to be due more to

[15] Hamer, *Quart. Rev.*, 1950, **4**, 327.
[16] Brooker, Sklar, Cressman, Keyes, Smith, Sprague, Van Lare, Van Zandt, White, and Williams, *J. Amer. Chem. Soc.*, 1945, **67**, 1875.
[17] Brooker, Dent, Heseltine, and Van Lare, *ibid.*, 1953, **75**, 4335.
[18] Brooker and Sprague, *ibid.*, 1941, **63**, 3203.

the contribution of the structure containing a positively charged $N_{(1)}$ atom than it is to that containing a positively charged $N_{(4)}$ atom, then the overall larger bathochromic shifts due to changes at the $N_{(1)}$ atom are explained. Finally, the effect of replacing a 3-methyl substituent by a 3-methylthio-substituent is seen to vary somewhat, but in all cases, *i.e.*, conversion of dye (1) into (2), of dye (3) into (5), and of dye (4) into (6), the bathochromic shifts are much smaller than those encountered above. This is understandable since the 3-position of the 1,2,4-triazole nucleus is not part of the mesomeric chain of the dye.

Experimental

All products are colourless unless otherwise stated.

5-Methyl-3-methylthio-1-phenyl-1,2,4-triazole.—(*a*) Phenylhydrazine (11·6 g.), methyl *N*-acetyldithiocarbamate [19] (16 g.), and benzene (100 c.c.) were refluxed for 2 hr. while the water formed was removed azeotropically. The benzene was evaporated and the residue dissolved in ether (200 c.c.). After being washed with 10% aqueous sodium hydroxide (3 × 50 c.c.), the ethereal solution was dried (K_2CO_3) and evaporated. Distillation of the residue gave the *triazole* as an orange liquid (10·5 g., 47·7%), b. p. 149—150°/2 mm. (Found: C, 58·2; H, 5·55; S, 15·2. $C_{10}H_{11}N_3S$ requires C, 58·5; H, 5·4; S, 15·6%).

(*b*) 3-Mercapto-5-methyl-1-phenyl-1,2,4-triazole [6] (1·9 g.), N-sodium hydroxide (10 c.c.), and methyl iodide (0·62 c.c.) were placed in a stoppered vessel, shaken for 1 hr. Extraction with ether (3 × 20 c.c.), etc., as above, gave the pure triazole (1·5 g., 75%), b. p. 150°/2 mm. (Found: C, 58·3; H, 5·4; C, 15·5%).

3-Ethylthio-5-methyl-1-phenyl-1,2,4-triazole was prepared by method (*a*) from phenylhydrazine (5·4 g.), ethyl *N*-acetyldithiocarbamate [19] (8·15 g.), and benzene (50 c.c.) and distilled as an orange liquid (4 g., 36·5%), b. p. 157—159°/0·1 mm. (Found: S, 14·4; N, 19·0. $C_{11}H_{13}N_3S$ requires S, 14·6; N, 19·2%).

3-Methylthio-1-phenyl-1,2,4-triazole.—3-Mercapto-1-phenyl-1,2,4-triazole [20] (14·3 g.), N-sodium hydroxide (81 c.c.), and methyl iodide (5·1 c.c.) were shaken for 1 hr., then extracted with chloroform (3 × 50 c.c.). The chloroform solution was dried (K_2CO_3) and evaporated. Distillation of the residue gave the *triazole* (11·4 g., 74%), b. p. 194—196°/15 mm., needles, m. p. 43° (Found: S, 16·5. $C_9H_9N_3S$ requires S, 16·75%).

5-Methylthio-3-methyl-1-phenyl-1,2,4-triazole.—5-Hydroxy-3-methyl-1-phenyl-1,2,4-triazole [21] (58 g.), phosphorus pentasulphide (74 g.), and toluene (500 c.c.) were refluxed for 3 hr. and filtered hot. On cooling, the filtrate deposited needles which recrystallised from benzene to give the *mercaptotriazole* (29 g., 45·3%) as needles, m. p. 182° (Found: S, 16·65. $C_9H_9N_3S$ requires S, 16·75%). The mercapto-compound (28 g.), N-sodium hydroxide (147 c.c.), and methyl iodide (9·2 c.c.) were shaken for 1 hr. and extracted with chloroform (3 × 100 c.c.). After drying (K_2CO_3), the chloroform was evaporated and the residue distilled to give the *methyltriazole* (26 g., 86·5%), b. p. 125—127°/0·15 mm., needles, m. p. 34° (Found: S, 15·5. $C_{10}H_{11}N_3S$ requires S, 15·6%).

5-Mercapto-3,4-dimethyl-1,2,4-triazole.—Acetic anhydride (48 c.c.) was added to 4-methylthiosemicarbazide [10] (50 g.), and the resulting hot solution was left for 1 hr. Dilution with water (60 c.c.) and cooling gave a solid which was recrystallised from water to give *acetyl-4-methylthiosemicarbazide* (50 g., 72%) as needles, m. p. 167° (decomp.) (Found: S, 21·7. $C_4H_9ON_3S$ requires S, 21·8%). The acetyl derivative (50 g.) was then added cautiously to a solution from sodium (9 g.) in ethanol (200 c.c.), and the mixture refluxed for 2 hr. After removal of the ethanol under reduced pressure, water (200 c.c.) was added and the solution filtered and acidified with concentrated hydrochloric acid (40 c.c.), to give a precipitate, which recrystallised from ethanol to give the pure *mercaptotriazole* (24 g., 55·8%) as needles, m. p. 210° (Found: S, 24·7. $C_4H_7N_3S$ requires S, 24·8%).

By similar methods, the following were obtained from the appropriate intermediates: *acetyl-4-ethylthiosemicarbazide* from ethanol as needles, m. p. 151° (45%) (Found: S, 20·1. $C_5H_{11}ON_3S$ requires S, 19·9%); *4-ethyl-3-methyl-5-mercapto-1,2,4-triazole* from ethanol as needles, m. p. 139° (65·7%) (Found: S, 22·6. $C_5H_9N_3S$ requires S, 22·4%); *acetyl-4-phenylthiosemicarbazide* which, being insoluble was crushed under ethanol to give needles, m. p. 170° (decomp.)

[19] Delépine, *Bull. Soc. chim. France*, 1903, **29**, 50.
[20] Pellizzari and Ferro, *Gazzetta*, 1898, **28**, 552.
[21] Andreocci, *ibid.*, 1889, **19**, 448.

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(74·5%) (Found: S, 16·25. $C_9H_{11}ON_3S$ requires S, 15·3%); *5-mercapto-3-methyl-4-phenyl-1,2,4-triazole* as an amorphous solid, m. p. 220° (44·7%) (Found: S, 16·8. $C_9H_9N_3S$ requires S, 16·75%), by dissolving the crude triazole in dilute aqueous ammonia and precipitating it with concentrated hydrochloric acid.

3,4-Dimethyl-5-methylthio-1,2,4-triazole.—5-Mercapto-3,4-dimethyl-1,2,4-triazole (19·35 g.), N-sodium hydroxide (150 c.c.), and methyl iodide (9·36 c.c.), shaken for 1 hr. and then extracted with chloroform (3 × 100 c.c.), gave the methylated *triazole* (11·4 g., 53·2%), b. p. 200°/14 mm., hygroscopic plates, m. p. 55—57° (Found: S, 22·6; N, 28·65. $C_5H_9N_3S$ requires S, 22·4; N, 29·4%).

By use of the appropriate intermediate and alkyl iodide the following alkylated *1,2,4-triazoles* were prepared similarly: *4-ethyl-3-methyl-5-methylthio*, b. p. 186—188°/10 mm. (67%) (Found: S, 20·4; N, 26·4. $C_6H_{11}N_3S$ requires S, 20·4; N, 26·75%); *3-methyl-5-methylthio-4-phenyl*, needles [from light petroleum (b. p. 100—120°)], m. p. 119° (70·7%) (Found: S, 15·4; N, 20·4. $C_{10}H_{11}N_3S$ requires S, 15·6; N, 20·5%); *5-ethylthio-3-methyl-4-phenyl*, needles [from light petroleum (b. p. 100—120°)], m. p. 106° (76·3%) (Found: S, 14·3; N, 18·7. $C_{11}H_{13}N_3S$ requires S, 14·6; N, 19·2%).

5-Ethylthio-3,4-dimethyl-1,2,4-triazole.—5-Mercapto-3,4-dimethyl-1,2,4-triazole (13 g.), 20% aqueous sodium hydroxide (60 c.c.), and ethyl sulphate (16·25 c.c.) were stirred for 1 hr., then heated on a steam-bath for 30 min. after which the mixture was cooled and extracted with chloroform (3 × 100 c.c.). The chloroform solution was dried (Na_2SO_4) and evaporated, and the residue distilled to give the *ethyltriazole* (7·3 g., 46·5%), b. p. 206°/12 mm. (Found: S, 19·8; N, 26·3. $C_6H_{11}N_3S$ requires S, 20·4; N, 26·75%).

3,4,5-Trimethyl-1,2,4-triazole.—As reported by us,[4] preparation of this triazole by Meyer's method,[22] gave a trihydrate. 2,5-Dimethyl-1,3,4-oxadiazole [23] (9·8 g.) and 10% w/v ethanolic methylamine (40 c.c.) at 100° (5 hr.) also the *trihydrate* (5·74 g., 35%), needles, m. p. 94° (Found: C, 36·15; H, 8·8; N, 25·15. Calc. for $C_5H_9N_3,3H_2O$: C, 36·35; H, 9·1; N, 25·45%). Keeping this *in vacuo* over phosphoric oxide for about 14 hr. (loss, 32·7, 33·0. Calc. for $3H_2O$: 32·75%) gave the anhydrous *triazole* which crystallised from anhydrous benzene in plates, m. p. 178° (Found: N, 37·7. $C_5H_9N_3$ requires N, 37·85%). This readily reverted to the trihydrate in air or on crystallising from water. By the method used by Meyer [22] for preparation of 3,5-dimethyl-4-phenyl-1,2,4-triazole were prepared: *4-p-methoxyphenyl-3,5-dimethyl-*, needles [from benzene–light petroleum (b. p. 40—60°) (3 : 2)], m. p. 180° (45%) (Found: N, 20·6. $C_{11}H_{13}ON_3$ requires N, 20·7%), and *4-p-chlorophenyl-3,4-dimethyl-1,2,4-triazole*, needles (from ethyl acetate), m. p. 236° (48%) (Found: Cl, 17·0. $C_{10}H_{10}N_3Cl$ requires Cl, 17·1%).

By refluxing a mixture of the appropriate triazole and methyl iodide (1 c.c. per g. of triazole; the reaction time is given in parentheses), adding anhydrous ether, filtering off the product, and recrystallising it, the following *1,2,4-triazole methiodides* were prepared: 3,5-dimethyl-1-phenyl- [3] (2 hr.), needles (from acetone), m. p. 167—168° (43%) (Found: I, 40·2. Calc. for $C_{11}H_{14}N_3I$: I, 40·3%); 3-methyl-1-phenyl- [1] (2 hr.), needles (from acetone), m. p. 183—185° (51%) (Found: I, 41·5. Calc. for $C_{10}H_{12}N_3I$: I, 42·2%); *5-methyl-3-methylthio-1-phenyl-* (3 hr.), prisms (from acetone), m. p. 131° (55%) (Found: I, 36·0. $C_{11}H_{14}N_3SI$ requires I, 36·6%); *3-methylthio-1-phenyl-* (20 hr.), needles (from ethanol), m. p. 186—188° (56·5%) (Found: I, 38·1. $C_{10}H_{12}N_3SI$ requires I, 38·1%); *3-methyl-5-methylthio-1-phenyl-* (60 hr.), needles (from ethanol), m. p. 153°, (51%) (Found: I, 36·5. $C_{11}H_{14}N_3SI$ requires I, 36·6%); *3,4-dimethyl-5-methylthio-* (1 hr.), needles (from acetone), m. p. 164—166° (60%) (Found: I, 44·2. $C_6H_{12}N_3SI$ requires I, 44·6%); *3,5-dimethyl-4-phenyl-* (1 hr.), needles [from acetone–ether (7 : 1)], m. p. 99—101° (67·5%) (Found: I, 39·7. $C_{11}H_{14}N_3I$ requires I, 40·3%); *4-p-methoxyphenyl-3,5-dimethyl* (3 hr.), needles [from acetone–ether (17 : 1)], m. p. 174—176° (57%) (Found: I, 36·6. $C_{12}H_{16}ON_3I$ requires I, 36·8%); *4-p-chlorophenyl-3,5-dimethyl-* (1 hr.), needles [from acetone–ether (2 : 1)], m. p. 206° (63%) (Found: I, 36·2. $C_{11}H_{12}N_3ClI$ requires I, 36·3%).

3,4,5-Trimethyl-1,2,4-triazole Methiodide.—3,4,5-Trimethyl-1,2,4-triazole (0·4 g.), methyl iodide (0·8 c.c.), and anhydrous benzene (10 c.c.) were refluxed for 4 hr., then cooled, and the resulting methiodide (0·5 g., 55%) was filtered off. This recrystallised from methanol–ether (1 : 2) as needles, m. p. and mixed m. p. with 1,3,5-trimethyl-1,2,4-triazole methiodide [24] 141° (Found: I, 50·7. Calc. for $C_6H_{12}N_3I$: I, 50·1%). The infrared absorptions of the two samples were identical.

[22] Meyer, D.R.-P. 574,944/1933.
[23] Stolle, *Ber.*, 1899, **32**, 797.
[24] Atkinson and Polya, *J.*, 1954, 141.

Anhydro-3-mercapto-4,5-dimethyl-1-phenyl-1,2,4-triazolium Hydroxide.—(*a*) 5-Methyl-3-methylthio-1-phenyl-1,2,4-triazole methiodide (1·77 g.) and pyridine (10 c.c.) were refluxed for 1 hr. and poured into water (50 c.c.). After cooling, the resulting *thione* was filtered off and recrystallised from water to give needles (0·22 g., 21%), m. p. 292—294° (Found: C, 58·2; H, 5·6; S, 15·6. $C_{10}H_{11}N_3S$ requires C, 58·5; H, 5·4; S, 15·6%), $\lambda_{max.}$ (in ethanol) 2450 Å (ε 17,220).

(*b*) 4-Methyl-1-phenylthiosemicarbazide [25] (4 g.), acetic acid (5 c.c.), and acetic anhydride (5 c.c.) were refluxed for 30 min. On cooling, the pure thione (3·5 g., 74%) crystallised as needles, m. p. and mixed m. p. 292—294° (Found: C, 58·9; H, 5·6; S, 15·85%).

Anhydro-3-mercapto-4-methyl-1-phenyl-1,2,4-triazolium Hydroxide.—(*a*) 3-Methylthio-1-phenyl-1,2,4-triazole methiodide (2·2 g.) and pyridine (10 c.c.) as above gave the *thione* (0·35 g., 28%), needles (from ethanol), m. p. 267—268° (Found: S, 16·8. $C_9H_9N_3S$ requires S, 16·75%), $\lambda_{max.}$ (in ethanol): 2480 Å (ε 24,540).

(*b*) 4-Methyl-1-phenylthiosemicarbazide (3 g.) and 98% w/w formic acid (10 c.c.) were refluxed for 24 hr. and poured into water (75 c.c.). Filtration and recrystallisation of the product from ethanol gave the thione (0·7 g., 41%) as needles, m. p. and mixed m. p. 267—268° (Found: S, 16·6%).

Anhydro-3-mercapto-1,4,5-trimethyl-1,2,4-triazolium Hydroxide.—3,4-Dimethyl-5-methylthio-1,2,4-triazole methiodide (1 g.) and pyridine (5 c.c.) was refluxed for 13 hr. and evaporated under reduced pressure. Recrystallisation of the residue from ethanol gave the *thione* (0·22 g., 44%) as needles, m. p. 257—259° (Found: S, 22·6. $C_5H_9N_3S$ requires S, 22·4%), $\lambda_{max.}$ (in ethanol) 2420 Å (ε 13,090).

4,5-*Dihydro-3,4-dimethyl-1-phenyl-1,2,4-triazole-5-thione.*—(*a*) 3-Methyl-5-methylthio-1-phenyl-1,2,4-triazole methiodide (4 g.) and pyridine (20 c.c.) were refluxed for 1 hr. and poured into water (50 c.c.). Filtration and recrystallisation from water gave the *thione* (0·85 g., 34%) as plates, m. p. 79—81° (Found: S, 15·7. $C_{10}H_{11}N_3S$ requires S, 15·6%), $\lambda_{max.}$ (in ethanol) 2870 Å (ε 10,250).

(*b*) 4-Methyl-2-phenylthiosemicarbazide [25] (8·2 g.) and glacial acetic acid (20·5 c.c.) were stirred at room temperature while acetic anhydride (5·1 c.c.) was added in one portion. After a further 30 minutes' stirring, the mixture was poured into water (100 c.c.), and the acetylated thiosemicarbazide was filtered off and recrystallised from ethyl acetate as needles (2·5 g., 25%), m. p. 166—168°. This compound (2·2 g.) was added to a solution from sodium (0·23 g.) in ethanol (20 c.c.), and the mixture refluxed for 2 hr. After cooling, the insoluble part was filtered off and recrystallised from water, to give the thione (1·5 g., 75%) as plates, m. p. and mixed m. p. 79—81° (Found: S, 15·8%).

2,3-*Dihydro-2,5-dimethyl-1-phenyl-1,2,4-triazole-3-thione.*—A solution of 1-methyl-2-phenylhydrazine (40 g.) in ethanol (40 c.c.) was treated cautiously with concentrated hydrochloric acid (33 c.c.) and then evaporated under reduced pressure. The residue was dried by azeotropic distillation with ethanol (2 × 50 c.c.), dissolved in ethanol (500 c.c.), and mixed with dried potassium thiocyanate (32 g.). After being refluxed for 15 hr., the mixture was filtered hot. The filtrate deposited 2-*methyl-1-phenylthiosemicarbazide* which recrystallised from alcohol as yellow needles (17·6 g., 30%), m. p. 200—202° (Found: C, 53·5; H, 6·1. $C_9H_{11}N_3S$ requires C, 53·0; H, 6·1%). The thiosemicarbazide (17·6 g.), acetic anhydride (9·5 c.c.), and acetic acid (40 c.c.) were refluxed for 1 hr., then poured into water to give the crude acetyl derivative (17·3 g., 80%) as buff needles, m. p. 184—188°. This was added to a solution from sodium (1·8 g.) in ethanol (100 c.c.), and the mixture refluxed for 15 hr. After cooling, the insoluble *thione* was filtered off and recrystallised from ethanol to give plates (10·8 g., 68%), m. p. 267—269° (Found: C, 58·6; H, 5·5; S, 15·6. $C_{10}H_{11}N_3S$ requires C, 58·5; H, 5·4; S, 15·6%), $\lambda_{max.}$ (in ethanol) 2910 Å (ε 12,812).

2,5-*Dimethyl-3-methylthio-1-phenyl-1,2,4-triazole Methiodide.*—2,3-Dihydro-2,5-dimethyl-1-phenyl-1,2,4-triazole-3-thione (1 g.) and methyl iodide (2 c.c.) were refluxed for 1 hr. and the crude *methiodide* was filtered off. Recrystallisation from acetone gave needles (1·1 g., 64%), m. p. 140—142° (Found: I, 36·2. $C_{11}H_{14}N_3SI$ requires I, 36·6%).

By similar methods, the following 1-*phenyl-1,2,4-triazole methiodides* were prepared from the corresponding thiones; they were identical (m. p. and mixed m. p.) with those prepared directly from the triazole bases: 5-*methyl-3-methylthio-1-phenyl-*, prisms (from acetone), m. p. 131° (79%) (Found: I, 36·6. $C_{11}H_{14}N_3SI$ requires I, 36·6%); 3-*methylthio-*, needles (from ethanol),

[25] Busch, Opfermann, and Walther, *Ber.*, 1904, **37**, 2332.

Trimethincyanines (XI; $m = 1$).

-C-D-N-R‴ *	R	R′	R″	X	Yield (%)	Solvent	M. p.	Formula	Required (%) C	Required (%) H	Required (%) Hal	Found (%) C	Found (%) H	Found (%) Hal
A	Me	Me	Me	ClO_4	20	MeOH [a]	240° (1)	$C_{17}H_{21}O_5N_4Cl$	—	—	8·95	—	—	8·9
A	Me	MeS	Me	I	20	H_2O [c]	214 (2)	$C_{17}H_{21}ON_4SI$	44·7	4·6	—	44·7	4·9	—
A	Me	Me	Ph	I	25	MeOH [a]	248—250 (3)	$C_{22}H_{23}ON_4I$ †	54·3	4·7	26·1	54·3	5·1	25·9
A	Ph	Me	Me	I	20	EtOH [c]	225 (4)	$2C_{22}H_{23}ON_4I,C_2H_5OH$	54·2	5·1	24·95	53·7	4·8	24·7
A	Me	MeS	Ph	I	23	EtOH [a]	236—237 (5)	$C_{22}H_{23}ON_4SI$	51·0	4·4	24·5	50·9	4·7	23·8
A	Ph	MeS	Me	I	14	EtOH [a]	220—222 (6)	$C_{22}H_{23}ON_4SI,H_2O$	—	—	23·7	—	—	23·8
B	Ph	Me	Me	I	36	MeOH [b]	247—248	$2C_{22}H_{23}N_4SI,CH_3{\cdot}OH$	52·1	4·8	24·5	52·2	4·7	24·8
B	Ph	MeS	Me	I	56	MeOH [b]	233—234	$2C_{22}H_{23}N_4S_2I,CH_3{\cdot}OH$	—	—	23·1	—	—	23·3
B	Ph	MeS	Me	I	36	MeOH [b]	233—234	$2C_{22}H_{23}N_4S_2I,CH_3{\cdot}OH$ †	—	—	23·1	—	—	23·3
B	Ph	EtS	Me	I	32	EtOH [b]	223—224	$2C_{23}H_{25}N_4S_2I,C_2H_5{\cdot}OH$	—	—	22·8	—	—	22·7
B	Me	MeS	Et	ClO_4	13	MeOH [b]	184—186	$C_{18}H_{23}O_4N_4S_2Cl,2CH_3{\cdot}OH$	—	—	6·8	—	—	6·85
B	Me	MeS	Ph	I	43	EtOH [c]	232—234	$2C_{22}H_{23}N_4S_2I,C_2H_5{\cdot}OH$	—	—	22·8	—	—	22·8
B	Me	EtS	Ph	I	24	MeOH [c]	225—227	$C_{23}H_{25}N_4S_2I,H_2O$	—	—	22·4	—	—	22·35
B	Me	MeS	Me	ClO_4	22	MeOH [d]	217—219	$C_{17}H_{21}O_4N_4S_2Cl$	(S, 14·4)			(S, 14·3)		
B	Me	Me	Ph	I	26	EtOH [b]	195	$C_{22}H_{23}N_4SI$ †	—	—	25·3	—	—	24·9
B	Me	Me	*p*-MeO·Ph	I	19	H_2O [b]	245	$C_{23}H_{25}ON_4SI,H_2O$ †	—	—	22·8	—	—	23·1
C	Ph	Me	Me	ClO_4	11	EtOH [b]	212—213	$C_{24}H_{27}O_4N_4Cl$	—	—	7·5	—	—	7·4
C	Ph	MeS	Me	ClO_4	20	MeOH [c]	220—221	$C_{24}H_{27}O_4N_4SCl$	—	—	7·1	—	—	7·2
C	Ph	EtS	Me	ClO_4	23	MeOH [c]	225	$C_{25}H_{29}O_4N_4SCl,2CH_3{\cdot}OH$	—	—	6·1	—	—	5·9
A	Ph	EtS	Me	I	9	H_2O [c]	202—203	$2C_{23}H_{25}ON_4SI,H_2O$	51·0	4·8	23·5	51·4	5·2	23·5
A	Me	EtS	Me	ClO_4	12	EtOH [a]	191	$C_{18}H_{23}O_5N_4SCl$	—	—	8·0	—	—	8·0
A	Me	MeS	Et	ClO_4	14	MeOH [a]	197	$C_{18}H_{23}O_5N_4SCl,CH_3{\cdot}OH$	—	—	7·5	—	—	7·4
A	Me	Me	*p*-MeO·Ph	I	22	EtOH [a]	261	$C_{23}H_{25}O_2N_4I$ †	—	—	24·6	—	—	24·5
E	Ph	Me	Me	I	25	EtOH [c]	231—232	$C_{24}H_{25}N_4I$	—	—	25·6	—	—	25·1

* A = 3-Ethyl-2-benzoxazole; B = 3-ethyl-2-benzothiazole; C = 1,3,3-trimethyl-2-indolenine; E = 1-ethyl-2-quinoline.

[a] Orange needles. [b] Purple needles. [c] Red needles. [d] Brown needles. [e] Yellow needles.

$\lambda_{max.}$ (in ethanol): (1) 3940 Å; (2) 4080 Å; (3) 4370 Å; (4) 4430 Å; (5) 4500 Å; (6) 4530 Å.

† From the triazole methiodide.

m. p. 186—188° (87%) (Found: I, 38·2. $C_{10}H_{12}N_3SI$ requires I, 38·1%); **3-*methyl*-5-*methylthio*-**, needles (from ethanol), m. p. 153° (98%) (Found: S, 9·4; I, 36·6. $C_{11}H_{14}N_3SI$ requires S, 9·2; I, 36·6%).

Degradation of 1,3,5-*Trimethyl*-1,2,4-*triazole Methiodide.*—The methiodide (5·9 g.) and 50% potassium hydroxide (40 c.c.) were refluxed for 2 hr. while the uncondensed vapours were passed through a tube of solid potassium hydroxide and thence into a solution of picric acid (5·4 g.) in anhydrous benzene (200 c.c.). The resulting methylamine picrate (1·7 g., 28%) was obtained as yellow needles, m. p. and mixed m. p. 208°. The residual alkaline solution was distilled and the distillate (15 c.c.) neutralised with 1·01N-sulphuric acid (25 c.c.). Addition of more 1·01N-sulphuric acid (25 c.c.) and evaporation of the solution under reduced pressure gave a crystalline residue which was dried by azeotropic distillation with ethanol (2 × 50 c.c.). Recrystallisation of the residue from methanol gave methylhydrazine sulphate (1·6 g., 54%) as needles, m. p. and mixed m. p. 144°.

Degradation of 3,5-*Dimethyl*-1-*phenyl*-1,2,4-*triazole Methiodide.*—The methylamine picrate (1·7 g., 33%) was recovered from the methiodide (6·3 g.) and 50% potassium hydroxide (20 c.c.) by the method used above. The residual alkaline mixture was diluted with water (30 c.c.) and distilled, and the distillate (30 c.c.) was treated with ethanol (5 c.c.), glacial acetic acid (2 c.c.), and benzaldehyde (2·1 c.c.) to give a crop of pale yellow needles. By repeating this process four times and recrystallising the assembled crops from ethanol, benzaldehyde phenylhydrazone (1·73 g., 45%) was obtained as pale yellow needles, m. p. and mixed m. p. 155—157°.

Conversion of 3,5-*Dimethyl*-1-*phenyl- and* 3-*Methyl*-5-*methylthio*-1-*phenyl*-1,2,4-*triazole into the Same Cyanine Dye.*—(*a*) 3,5-Dimethyl-1-phenyl-1,2,4-triazole (0·35 g.), methyl toluene-*p*-sulphonate (0·74 g.), and 2-methylthiobenzothiazole (0·36 g.) were fused for 1 hr. at 140°. Pyridine (5 c.c.) and triethylamine (2 c.c.) were added, the mixture was refluxed for 1 hr. and then poured into 4% aqueous sodium iodide (50 c.c.). The precipitate was filtered off, washed with ether, and recrystallised from ethanol, to give the *dye* (XI; D = the residue of a benzothiazole nucleus, R = Ph, R′ = R″ = R‴ = Me, *m* = 0, X = I) (0·23 g., 24%) as yellow leaflets, m. p. 207—209° (Found: I, 26·2. $C_{19}H_{19}N_4SI,H_2O$ requires I, 26·5%).

(*b*) By the same method, 3-methyl-5-methylthio-1-phenyl-1,2,4-triazole (0·62 g.), methyl toluene-*p*-sulphonate (1·12 g.), and 2-methylbenzothiazole (0·45 g.) gave the same dye (0·2 g., 14%), m. p. and mixed m. p. 207—209° (Found: I, 26·5%). The dye (0·1 g., 11%) was also obtained by refluxing a mixture of this methiodide (0·69 g.), 2,3-dimethylbenzothiazolium iodide (0·58 g.), pyridine (5 c.c.), and triethylamine (2 c.c.) for 1 hr., and then proceeding as above (Found: I, 26·4%).

4-[2-(3,4-*Dimethyl*-1-*phenyl*-1,2,4-*triazolin*-5-*ylidene*)*ethylidene*]-2-*phenyl*-5-*oxazolone*.—3,5-Dimethyl-1-phenyl-1,2,4-triazole (0·35 g.) and methyl toluene-*p*-sulphonate (0·37 g.) were fused for 1 hr. at 140°, then mixed with 4-ethoxymethylene-2-phenyl-5-oxazolone (0·43 g.), pyridine (5 c.c.), and triethylamine (2 c.c.). The mixture was refluxed for 1 hr. and poured into water (50 c.c.). The precipitate was filtered off and recrystallised from ethanol, to give the *dye* (0·24 g., 33%) as orange needles, m. p. 257—259° (Found: N, 15·3. $C_{21}H_{15}O_2N_4$ requires N, 15·6%).

By similar methods, the appropriate triazole and the oxazolone or 5-ethoxymethylene-3-ethyl-2-thiothiazolid-4-one gave **4-[2-(4-*methyl*-3-*methylthio*-1-*phenyl*-1,2,4-*triazolin*-5-*ylidene*)-*ethylidene*]-2-*phenyl*-5-*oxazolone***, red needles (from ethanol), m. p. 241—242° (25%) (Found: N, 12·2. $2C_{21}H_{18}O_2N_4S,3C_2H_5{\cdot}OH$ requires N, 12·2%), and **3-*ethyl*-5-[2-(3-*ethylthio*-1-*methyl*-4-*phenyl*-1,2,4-*triazolin*-5-*ylidene*)*ethylidene*]-2-*thiothiazolid*-4-*one***, red needles (from ethanol), m. p. 229° (40%) (Found: N, 13·3. $2C_{18}H_{20}ON_4S_3,C_2H_5{\cdot}OH$ requires N, 13·2%).

The following merocyanines were made from the triazole methiodides: **3-*ethyl*-5-[2-(3,4-*dimethyl*-1-*phenyl*-1,2,4-*triazolin*-5-*ylidene*)*ethylidene*]-2-*thiothiazolid*-4-*one***, brown needles (from methanol), m. p. 231° (28%) (Found: S, 17·9. $C_{17}H_{18}ON_4S_2$ requires S, 17·9%); **3-*ethyl*-5-[2-(1,4-*dimethyl*-3-*methylthio*-1,2,4-*triazolin*-5-*ylidene*)*ethylidene*]-2-*thiothiazolid*-4-*one***, orange needles (from ethanol), m. p. 238° (30%) (Found: N, 16·1. $2C_{12}H_{16}ON_4S_3,C_2H_5{\cdot}OH$ requires N, 15·95%); **3-*ethyl*-5-[2-(4-p-*methoxyphenyl*-1,3-*dimethyl*-1,2,4-*triazolin*-5-*ylidene*)*ethylidene*]-2-*thiothiazolid*-4-*one***, bronze plates (from ethanol), m. p. 229° (21%) (Found: N, 11·3. $C_{18}H_{20}O_2N_4S_2,2C_2H_5{\cdot}OH$ requires N, 11·7%); **5-[2-(4-p-*chlorophenyl*-1,3-*dimethyl*-1,2,4-*triazolin*-5-*ylidene*)*ethylidene*]-3-*ethyl*-2-*thiothiazolid*-4-*one***, red plates (from ethanol), m. p. 259—261° (35%) (Found: N, 13·9. $C_{17}H_{17}ON_4S_2Cl$ requires N, 14·3%).

5-*Ethoxymethylene*-3-*ethyl*-2-*thiothiazolid*-4-*one* was prepared as follows: 3-ethyl-2-thiothiazolid-4-one (32 g.), ethyl orthoformate (40 c.c.), and acetic anhydride (60 c.c.) were refluxed

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for 18 hr. After cooling, the product was filtered off and recrystallised from ethanol forming yellow needles (22 g., 50%), m. p. 94° (Found: S, 29·5. $C_8H_{11}O_2NS_2$ requires S, 29·5%).

The following monomethincyanines (XI; $m = 0$) were prepared by a joint fusion process similar to that described earlier for the preparation of the dye (XI; D = residue of a benzothiazole nucleus, R = Ph, R′ = R″ = R‴ = Me, $m = 0$, X = I): (*1,3,4-trimethyl-5-1,2,4-triazole*)(*3-methyl-2-benzothiazole*)*monomethincyanine perchlorate* buff-coloured needles (from water), m. p. 235° (16%) (Found: Cl, 9·2. $C_{14}H_{17}O_4N_4SCl$ requires Cl, 9·1%); (*4-methyl-3-methylthio-1-phenyl-5-1,2,4-triazole*)(*3-methyl-2-benzothiazole*)*monomethincyanine iodide*, buff-coloured needles (from ethanol), m. p. 132—134° (10%) (Found: I, 23·3. $C_{19}H_{19}N_4S_2I,C_2H_5{\cdot}OH$ requires I, 23·5%); (*1,4-dimethyl-2-methylthio-5-1,2,4-triazole*)(*3-methyl-2-benzothiazole*)*monomethincyanine perchlorate*, yellow leaflets (from methanol), m. p. 236—237° (50%) (Found: S, 16·0. $C_{14}H_{17}O_4N_4S_2Cl$ requires S, 15·8%).

The trimethincyanines (XI; $m = 1$) contained in the Table were prepared by fusing the triazole and methyl toluene-*p*-sulphonate for 1 hr. at 140° and then refluxing the salt, the appropriate 2-2′-acetanilidovinyl heterocyclic quaternary salt, pyridine, and triethylamine for 1 hr. and pouring the whole into 4% aqueous sodium iodide or perchlorate. Numbers which have been given to the first six dyes correspond to those of the dyes discussed in the theoretical part.

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Renwick Laboratory, Ilford Limited,
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767. *Modified Steroid Hormones. Part XIII.* Some Propargyl Derivatives.*

By D. Burn, G. Cooley, V. Petrow, and G. O. Weston.

The preparation of the 2α- (I; R = α-$CH_2{\cdot}C{\equiv}CH$, R′ = H) and 6α-propargyl (IV; R = OH, R′ = H) derivatives of testosterone and the 6α-propargyl derivatives of progesterone (IV; R = Ac, R′ = H) and 17α-acetoxyprogesterone (IV; R = Ac, R′ = OAc) is reported.

Work on methylated steroid hormones [1,2] is herein extended to the preparation of some propargyl derivatives.

Condensation of testosterone with ethyl formate [3] in the presence of sodium hydride afforded 2-formyltestosterone (I; R = CHO, R′ = H), which was treated without purification with propargyl bromide. Elimination of the formyl group from the intermediate (I; R = CHO, R′ = $CH_2{\cdot}C{\equiv}CH$) with sodium hydroxide led to the required 2α-propargyltestosterone (I; R = α-$CH_2{\cdot}C{\equiv}CH$, R′ = H) (characterised as the 17-acetate). The structure assigned to the last compound was supported by the infrared spectrum which (in CCl_4) showed bands at 3312 (≡C·H), 2104 (C≡C), 1736 (OAc), 1675, and 1619 $cm.^{-1}$ (Δ^4-3-one).

Preparation of 6α-propargyltestosterone (IV; R = OH, R′ = H) was achieved by extension of the general method developed in Part VII.[2] 5α,6α-Epoxy-3,3-ethylenedioxy-5α-androstan-17β-ol [2] (II; R = OH, R′ = H) with propargylmagnesium bromide furnished

* Part XII, *J.*, 1959, 3595, which paper was incorrectly numbered Part XI (cf. *J.*, 1959, 788).

[1] Burn, Ellis, Petrow, Stuart-Webb, and Williamson, *J.*, 1957, 4092; Ackroyd, Adams, Ellis, Petrow, and Stuart-Webb, *ibid.*, p. 4099.
[2] Cooley, Ellis, Kirk, and Petrow, *J.*, 1957, 4112; B.P. 809,465/1959; cf. Campbell, Babcock, and Hogg, *J. Amer. Chem. Soc.*, 1958, **80**, 4717.
[3] Quartey, *J.*, 1958, 1710.

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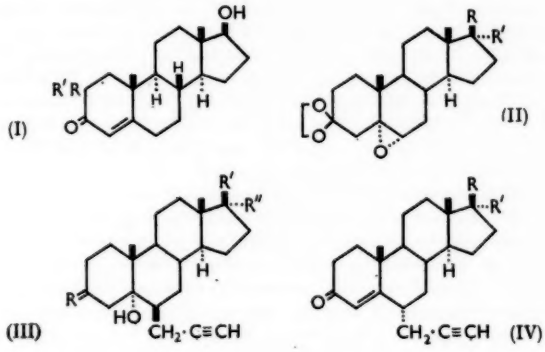
3,3-ethylenedioxy-6β-propargyl-5α-androstane-5α,17β-diol (III; R = ethylenedioxy, R′ = OH, R″ = H) which passed smoothly into the corresponding ketone (III; R = O, R′ = OH, R″ = H) on treatment with aqueous acetic acid. Dehydration with ethanolic hydrochloric acid afforded a product regarded as 6α-propargyltestosterone (IV; R = OH, R′ = H) by analogy with the formation of 6α-methylated steroid hormones under similar experimental conditions.[1,2] No attempt was made to prepare the 6β-isomer as, in general, 6β-alkylated hormones are less potent biologically than their 6α-alkyl analogues. Application of the same reaction sequence to 3,3:20,20-bisethylenedioxy-5α,6α-epoxy-5α-pregnane[3] (II; R = 1,1-ethylenedioxyethyl, R′ = H) led to the intermediates (III; R = ethylenedioxy, R′ = 1,1-ethylenedioxyethyl, R′ = H) and (III; R = O, R′ = Ac,



R″ = H) and thence to 6α-propargylprogesterone (IV; R = Ac, R′ = H). Evidence for the α-configuration of the propargyl group was obtained from the *R*-band spectrum. It has been shown[4] that 6β-substitution by halogen and acyloxy-groups produces a bathochromic shift of *ca.* 15 mμ of the fine-structure bands of steroidal Δ^4-3-ones, whilst 6α-substitution produces a negligible shift. We find[5] the same pattern of behaviour to apply to 6-methyl substituents although in this case the shifts are somewhat smaller. As the *R*-band spectrum of 6α-propargylprogesterone (IV; R = Ac, R′ = H) is virtually identical with that of progesterone it seems reasonable to conclude that, in this compound too, the 6-substituent has the α-configuration. Unfortunately, extension of such measurements to the other 6-propargyl steroids described herein did not prove possible owing to their limited solubility in suitable organic solvents.

Finally, attention was directed to the preparation of the 6α-propargyl analogue of the progestationally active substance, 17α-acetoxy-6α-methylprogesterone.[6,7] 3,3:20,20-Bisethylenedioxy-5α,6α-epoxy-5α-pregnan-17α-ol[6] (II; R = 1,1-ethylenedioxyethyl, R′ = OH) was treated with propargylmagnesium bromide, and the resulting product (III; R = ethylenedioxy, R′ = 1,1-ethylenedioxyethyl, R″ = OH) was hydrolysed with aqueous-methanolic oxalic acid, to yield 5α,17α-dihydroxy-6β-propargyl-5α-pregnane-3,20-dione (III; R = O, R′ = Ac, R″ = OH). Dehydration with ethanolic hydrochloric acid afforded 17α-hydroxy-6α-propargylprogesterone (IV; R = Ac, R′ = OH) which passed into the required 17α-acetoxy-6α-propargylprogesterone (IV; R = Ac, R′ = OAc) on forced acetylation.[8]

Biological results will be reported elsewhere.

[4] Bird, Cookson, and Dandegaonker, *J.*, 1956, 3675.
[5] With Mr. M. T. Davies, B.Sc., unpublished work.
[6] Babcock, Gutsell, Herr, Hogg, Stuki, Barns, and Dulin, *J. Amer. Chem. Soc.*, 1958, **80**, 2904.
[7] Sala, Camerino, and Cavallero, *Acta Endocrinol.*, 1958, **29**, 508.
[8] Turner, *J. Amer. Chem. Soc.*, 1953, **75**, 3489.

Experimental

M. p.s are corrected. Optical rotations were determined for chloroform solutions. Ultraviolet (in ethanol) and infrared spectra were kindly determined by Mr. M. T. Davies, B.Sc., and Miss D. F. Dobson, B.Sc.

2α-Propargyltestosterone (; R = α-CH_2·C:CH, R′ = H).—A solution of testosterone (5·75 g.) in ethyl formate (5 ml.) and dry benzene (100 ml.) containing sodium hydride (1·5 g.) was stirred under nitrogen at room temperature for 2 days. Dilution with water and extraction with ether yielded unchanged testosterone (1 g.). Ether-extraction of the acidified aqueous phase yielded 2-formyltestosterone as a gum (4·1 g.) which was treated in dry acetone (200 ml.) containing propargyl bromide (4 ml.) with potassium carbonate (1·2 g.). The mixture was then refluxed under nitrogen for 14 hr. The product (I; R = CHO, R′ = CH_2·C:CH) (5·4 g.), obtained by dilution with water and extraction in ether, was kept overnight under nitrogen at room temperature in methanol (100 ml.) and water (5 ml.) containing sodium hydroxide (4 g.). The product was isolated with ether and filtered in benzene solution through a short column of alumina (15 g.). Crystallisation from aqueous methanol yielded *2α-propargyltestosterone* as needles, m. p. 137—139°, $[\alpha]_D^{20}$ +60·7° (*c* 0·8), $\lambda_{max.}$ 241 mμ (log ε 4·19) (Found: C, 81·2; H, 9·55. $C_{22}H_{30}O_2$ requires C, 81·0; H, 9·25%). The *acetate* crystallised from aqueous methanol in rods, m. p. 141—143°, $[\alpha]_D^{25}$ +50·9° (*c* 0·8), $\lambda_{max.}$ 241 mμ (log ε 4·18) (Found: C, 77·7; H, 8·8. $C_{24}H_{32}O_3$ requires C, 78·2; H, 8·75%).

3,3-Ethylenedioxy-6β-propargyl-5α-androstane-5α,17α-diol.—A solution of the ketal epoxide [3] (II; R = OH, R′ = H) (3 g.) in dry benzene (100 ml.) was added to the Grignard reagent prepared from propargyl bromide (7 ml.) and magnesium (2 g.) in dry ether (75 ml.) with mercuric chloride [9] as initiator. It was necessary to add the steroid as soon as the Grignard reagent had been prepared since the latter was unstable. After the mixture had been kept at room temperature overnight, aqueous ammonium chloride was added to the cooled (0°) solution, and the product was isolated with ether. Chromatography on alumina (60 g.) in benzene gave the *ketal monohydrate* as needles [from ether–light petroleum (b. p. 40—60°)], m. p. 204°, $[\alpha]_D^{21}$ −70·5° (*c* 0·65) (Found: C, 70·65; H, 9·25. $C_{24}H_{36}O_4,H_2O$ requires C, 70·9; H, 9·4%). Prolonged drying of this material *in vacuo* at 150° yielded the hemihydrate (Found: C, 72·15; H, 9·75. $C_{24}H_{36}O_4,\frac{1}{2}H_2O$ requires C, 72·5; H, 9·4%).

5α,17β-Dihydroxy-6β-propargyl-5α-androstan-3-one (III; R = O, R′ = OH, R″ = H).—The foregoing ketal (1·08 g.) was kept at room temperature overnight in acetic acid (35 ml.) and water (1 ml.). The product was isolated with ether and crystallised from acetone–hexane to give the *ketone* as laths, m. p. 194—195°, $[\alpha]_D^{20}$ −50·8° (*c* 0·59) (Found: C, 76·3; H, 9·3. $C_{22}H_{32}O_3$ requires C, 76·7; H, 9·35%). The *acetate* crystallised from aqueous methanol in needles, m. p. 175—177°, $[\alpha]_D^{22}$ −42·1° (*c* 0·36) (Found: C, 74·2; H, 8·8. $C_{24}H_{34}O_4$ requires C, 74·6; H, 8·9%).

6α-Propargyltestosterone (IV; R = OH, R′ = H).—The ketone (III; R = O, R′ = OH, R″ = H) (0·17 g.) in ethanol (20 ml.) containing concentrated hydrochloric acid (0·1 ml.) was heated under reflux for 20 min. Dilution with water and recrystallisation of the product from aqueous ethanol gave *6α-propargyltestosterone* as needles, m. p. 163—165°, $[\alpha]_D^{20}$ +94·8° (*c* 0·8), $\lambda_{max.}$ 239·5 mμ (log ε 4·19) $\nu_{max.}$ (in CCl_4) 3634 (OH), 3327 (:C·H), 2121 (C:CH), 1688, 1616 $cm.^{-1}$ (Δ^4-3-one) (Found: C, 81·3; H, 9·5. $C_{22}H_{30}O_2$ requires C, 80·9; H, 9·3%).

5α-Hydroxy-6β-propargyl-5α-pregnane-3,20-dione (III; R = O, R′ = Ac, R″ = H).—The bis-ketal epoxide [3] (II; R = 1,1-ethylenedioxyethyl, R′ = H) (10 g.) in dry benzene (300 ml.) was added with stirring to the Grignard reagent prepared from propargyl bromide (10 ml.) and magnesium (3 g.) in dry ether (100 ml.), and the mixture was kept overnight at room temperature. The bisethylenedioxy-alcohol (14 g.), isolated in the usual way, was kept for 1 hr. at room temperature in methanol (150 ml.) and water (30 ml.) containing oxalic acid dihydrate (7 g.). The solid obtained on dilution with water recrystallised from chloroform–ethanol, to give *5α-hydroxy-6β-propargyl-5α-pregnane-3,20-dione* as prisms, m. p. 231—233°, $[\alpha]_D^{22}$ +29·5° (*c* 0·95) (Found: C, 77·4; H, 9·2. $C_{24}H_{34}O_3$ requires C, 77·8; H, 9·25%).

6α-Propargylprogesterone (IV; R = Ac, R′ = H).—The foregoing hydroxy-diketone (4·65 g.) was refluxed for 1 hr. in ethanol (100 ml.) containing concentrated hydrochloric acid (0·4 ml.). *6α-Propargylprogesterone* was precipitated with water and crystallised from aqueous ethanol as plates, m. p. 130—131°, $[\alpha]_D^{20}$ +177·6° (*c* 1·03), $\lambda_{max.}$ 240 mμ (log ε 4·17), $\lambda_{max.}$ (in cyclohexane) 323

[9] Cf. Renaud, *Bull. Soc. chim. France*, 1950, 1044.

(ε 43), 338 (ε 41), 351 (ε 30) and 369 mμ (ε 10), [progesterone in cyclohexane shows $\lambda_{max.}$ 321 (ε 41), 338 (ε 38), 351 (ε 28) and 367 mμ (ε 11)], $\nu_{max.}$ (in CCl_4) 3315 (≡C·H), 2117 (·C≡CH), 1713 (20-one), 1686 and 1614 cm.$^{-1}$ (Δ^4-3-one) (Found: C, 81·8; H, 9·0. $C_{24}H_{32}O_2$ requires C, 81·8; H, 9·15%).

5α,17α-Dihydroxy-6β-propargyl-5α-pregnane-3,20-dione (III; R = O, R′ = Ac, R″ = OH).—The bis-ketal epoxide [6] (II; R = 1,1-ethylenedioxyethyl, R′ = OH) (11 g.) in dry benzene (350 ml.) was added with stirring to the Grignard reagent prepared from propargyl bromide (14 ml.) and magnesium (4 g.) in dry ether (150 ml.), and the mixture kept overnight at room temperature. The bisethylenedioxy-alcohol (14·2 g.), isolated in the usual way, was kept for 2 hr. at room temperature in methanol (200 ml.) and water (25 ml.) containing oxalic acid dihydrate (7 g.). *5α,17α-Dihydroxy-6β-propargyl-5α-pregnane-3,20-dione* was precipitated with water and crystallised from dichloromethane–methanol as plates, m. p. 213—215°, $[\alpha]_D^{25}$ −61·1° (*c* 1·02), $\nu_{max.}$ (in Nujol) 3576, 3425 (OH), 3278 (≡C·H), 1712 (3- and 20-one), and 1690 cm.$^{-1}$ (17-OH, 20-one) * (Found: C, 74·0; H, 9·1. $C_{24}H_{34}O_4$ requires C, 74·5; H, 8·9%).

17α-Hydroxy-6α-propargylprogesterone (IV; R = Ac, R′ = OH).—The foregoing dihydroxy-diketone (4·3 g.) was refluxed for 1 hr. in ethanol (100 ml.) containing concentrated hydrochloric acid (0·4 ml.). The *product* was precipitated with water and crystallised from aqueous methanol as prisms, m. p. 164—166°, $[\alpha]_D^{23}$ +75·1° (*c* 1·79), $\lambda_{max.}$ 240 mμ, log ε 4·17, $\nu_{max.}$ (in Nujol) 3445 (OH), 3250 (≡C·H), 1700 (20-one), 1644 and 1599 cm.$^{-1}$ (Δ^4-3-one), $\nu_{max.}$ (in CH_2Cl_2) 1668, and 1608 cm^{-1} (Found: C, 78·1; H, 8·4. $C_{24}H_{32}O_3$ requires C, 78·2; H, 8·75%).

This compound (1·75 g.) in acetic acid (90 ml.) and acetic anhydride (20 ml.) containing toluene-*p*-sulphonic acid (0·8 g.) was stirred at room temperature for 4 hr. with initial cooling. The *acetate*, isolated with ether, was crystallised from aqueous methanol as prisms, m. p. 180—182°, $[\alpha]_D^{22}$ +66·8° (*c* 1·8), $\lambda_{max.}$ 239 mμ, log ε 4·18, $\nu_{max.}$ (in Nujol) 3301 (≡C·H), 2112 (C≡CH) 1741, 1246 (OAc), 1722 (20-one), 1671 and 1614 cm.$^{-1}$ (Δ^4-3-one) (Found: C, 75·6; H, 8·3. $C_{26}H_{34}O_4$ requires C, 76·1; H, 8·35%).

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CHEMICAL RESEARCH LABORATORIES, THE BRITISH DRUG HOUSES LTD.,
LONDON, N.1. [*Received, June 8th*, 1959.]

* Compounds containing the 17α-hydroxy-20-ketone system often show an " extra " carbonyl band around 1690 cm.$^{-1}$ due to hydrogen-bonding.[10]

[10] Jones, Humphries, Herling, and Dobriner, *J. Amer. Chem. Soc.*, 1952, **74**, 2820.

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768. *Isotope and Crystal-field Effects in the Vibrational Spectrum of Potassium Tetrafluoroborate.*

By N. N. GREENWOOD.

Comparison of the infrared spectra of normal and ^{10}B-enriched potassium tetrafluoroborate suggests that complexities in the vibrational spectrum of this compound arise both from an isotope doubling in the ν_3 and ν_4 fundamentals of the tetrahedral BF_4^- ion and from the removal of vibrational degeneracy of the ν_3 band as a result of interaction of the tetrahedral ion with a crystal field of lower symmetry. This distortion also permits the forbidden ν_1 symmetrical breathing mode to absorb weakly. Bands near 1310 and 1650 cm.$^{-1}$ are assigned as the combinations $(\nu_1 + \nu_4)$ and $(\nu_3 + \nu_4)$ respectively. The possibility of Fermi resonance between $2\nu_4$ and ν_3 is also considered.

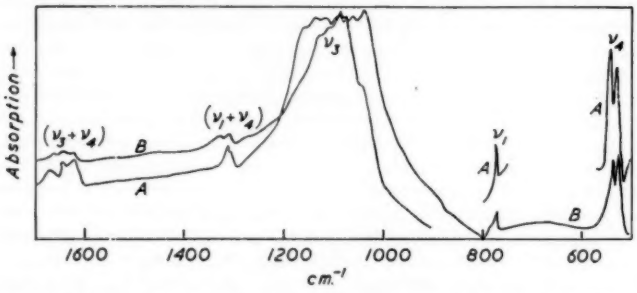
A REGULAR tetrahedral ion MX_4^- has only two infrared-active fundamentals, ν_3 and ν_4, and these are both triply degenerate.[1] The infrared spectrum of potassium tetrafluoroborate was investigated in the region 555—1665 cm.$^{-1}$ by Duval and Lecomte [2] who found only two maxima, a strong, broad band near 990 cm.$^{-1}$ (assigned as ν_3) and a relatively

[1] Herzberg, " Infrared and Raman Spectra of Polyatomic Molecules," D. van Nostrand Co. Inc., 1945.

[2] Duval and Lecomte, *Bull. Soc. chim. France*, 1947, **14**, 1057.

weak band at 1535 cm.$^{-1}$ ($\nu_3 + \nu_4$). By difference, ν_4 was obtained as 545 cm.$^{-1}$ though this band was not directly observed. Further work by Coté and Thompson [3] in the region 400—5000 cm.$^{-1}$, using both sublimed films and paraffin mulls at room temperature and at −183°, revealed that the strong, broad ν_3 band had two maxima and two shoulders

FIG. 1. *Infrared spectra of (A) ^{10}B-enriched and (B) normal potassium tetrafluoroborate.*



between 1000 and 1100 cm.$^{-1}$. In addition, there was a weak band at 771 cm.$^{-1}$ (assigned as the Raman-active ν_1 vibration) and a doublet at 521, 534 cm.$^{-1}$, assigned as ν_4. Combination bands were observed at 1302, 1784, and 2148 cm.$^{-1}$. The complex structure of the fundamentals ν_3 and ν_4 was discussed in terms of the isotopic species boron-10 and boron-11, and in relation to the possibility of removing the vibrational degeneracy which which may arise when a tetrahedral ion is situated in a crystal field of lower symmetry. Various arguments were considered and it was concluded, at that time, that it was impossible to decide between the two alternative interpretations. These difficulties have now mainly been resolved by investigating the infrared spectra of normal potassium tetrafluoroborate and of potassium tetrafluoroborate isotopically enriched in boron-10.

EXPERIMENTAL and RESULTS

The absorption spectrum of potassium tetrafluoroborate was recorded in the range 375—4000 cm.$^{-1}$ by means of a Unicam SP.100 spectrometer. Both Nujol mulls and potassium bromide discs (1—4 mg. of KBF_4/400 mg. of KBr) were used; the results were very similar over most of the spectrum but resolution within the ν_3 band appeared to be somewhat better with the disc technique.

Potassium tetrafluoroborate with a stated isotopic abundance ratio ^{10}B : ^{11}B of 9 : 1 was supplied by 20th Century Electronics, Ltd. The ^{10}B : ^{11}B ratio in normal potassium tetrafluoroborate (B.D.H) is 1 : 4. Both compounds were dried at 120° before use.

The two spectra are reproduced in Fig. 1. The vertical axis has been adjusted to give

Vibration bands of potassium tetrafluoroborate (R.I. = *relative intensity*)

	KBF_4 (20% ^{10}B)		KBF_4 (90% ^{10}B)				KBF_4 (20% ^{10}B)		KBF_4 (90% ^{10}B)		
Ref. 3	ν (cm.$^{-1}$)	R.I.	ν (cm.$^{-1}$)	R.I.	Assgt.	Ref. 3	ν (cm.$^{-1}$)	R.I.	ν (cm.$^{-1}$)	R.I.	Assgt.
521	525	8·3	530	14·2	ν_4^{11}	1302	1312	1·4	1305	1·9	$(\nu_1 + \nu_4)$
534	536	7·4	542	16·1	ν_4^{10}	(1305)	1330	1·3	1312	2·2	
771	773	2·3	773	0·8	ν_1 *		1623	0·9	1622	2·4	
1032	1038	26·5	1042	16·0		1784	1644	1·1	1644	2·0	$(\nu_3 + \nu_4)$
1058	1063	25·6	—	—			1671	0·7	1668	1·1	
1072	1078	25·5	1073	25·1		2148	2340	1·1	2335?	0·3	‡
(1090)	1088	26·2	1086	25·2	†	—	2925	1·3	2930	1·4	?
—	1107	23·9	1115	25·2							
—	1128	22·5	1135	25·2							
—	—	—	1158	23·8							

* Forbidden. † ν_3^{11} and ν_3^{10} with triple degeneracy removed; possibly also some $2\nu_4$. ‡ Possibly $2\nu_3$, $(2\nu_4 + \nu_3)$.

[3] Coté and Thompson, *Proc. Roy. Soc.*, 1951, *A*, **210**, 217.

comparable peak heights in the region of the ν_3 absorption. A different scale was used to plot the spectrum of the ^{10}B-enriched sample below 900 cm.$^{-1}$ in order to avoid congestion of the diagram. Enrichment in ^{10}B enhances the relative peak height of the high-frequency component of the ν_4 doublet and has a similar effect on the shape of the ν_3 band. The position and shape of the forbidden ν_1 singlet remains unaltered. The frequencies and relative intensities of the absorption maxima are given more precisely in the Table which also compares the present results with those of Coté and Thompson.[3]

Discussion

A molecule or ion containing n atoms has $3n-6$ normal modes of vibration. For a regular tetrahedral ion (symmetry T_d), there are nine modes distributed as follows: (1) a single vibration ν_1 of symmetry class A_1, Raman-active only; (2) a doubly degenerate deformation ν_2 of class E, Raman-active only; (3) a triply degenerate vibration ν_3 (class F_2), active in both Raman and infrared regions; and (4) a triply degenerate deformation ν_4 (class F_2) active in both Raman and infrared regions. These modes are illustrated in Fig. 2.

An isolated BF_4^- ion has zero dipole moment. As the ν_1 and ν_2 modes leave this moment unchanged they are forbidden infrared vibrations. The two triply degenerate modes ν_3 and ν_4, however, confer a resultant dipole on the ion and are thus infrared-active. Moreover, since the central atom moves in both these modes the frequency of ν_3 and ν_4 should, in principle, depend on the isotopic mass of the boron atom, though the shift in frequency might be too small to be resolved. If the tetrahedral ion is placed in a crystal field of lower symmetry the symmetrical ν_1 breathing frequency might be sufficiently distorted to permit weak absorption. Similarly, in a non-cubic field the co-ordinates x, y, and z in Fig. 2 are no longer arbitrarily interchangeable since motion along each axis is subject to a different potential field, *i.e.*, the vibrations are no longer degenerate. Potassium tetrafluoroborate has orthorhombic crystal symmetry, D_{2h}^{16}–*Pnma* with $a = 7{\cdot}85$, $b = 5{\cdot}68$, and $c = 7{\cdot}37$ Å,[4] and it is of interest to establish whether this reduction in symmetry is sufficient to remove the threefold degeneracy of the ν_3 and ν_4 modes.

Coté and Thompson [3] pointed out that the observed splittings of the ν_3 and ν_4 bands were consistent with the Teller–Redlich product rule for isotope effects,[1] but that the ν_3 band appeared to be split into at least four components and that the peak heights of the two ν_4 components were not in the ratio 1 : 4 as expected from the isotopic abundance ratio of boron-10 and -11. Difficulties were also encountered in attempting to explain the appearance of the bands exclusively in terms of removal of vibrational degeneracy and they were unable to decide between the two alternative interpretations. The present results resolve this difficulty by indicating that the two effects occur simultaneously. This leads to the following interpretation of the infrared spectrum of potassium tetrafluoroborate:

(1) The intense, polarized Raman line observed [5] at 769 cm.$^{-1}$ clearly corresponds to the ν_1 mode. This is a forbidden transition in the infrared region but is weakly [1] permitted in crystalline potassium tetrafluoroborate because of the perturbing influence of the crystal field on the tetrahedral BF_4^- ion. As the boron atom does not move in this mode (Fig. 2) its isotopic mass is unimportant and the absorption occurs as a single, narrow band at 773 cm.$^{-1}$ independently of the abundance ratio ^{10}B : ^{11}B.

(2) The doubly degenerate ν_2 mode has been observed [5] as a weak Raman line at 353 cm.$^{-1}$. It falls outside the wavelength region investigated here and, in the absence of a distorting crystal field, is forbidden in the infrared region. No overtones or combinations of this band were observed.

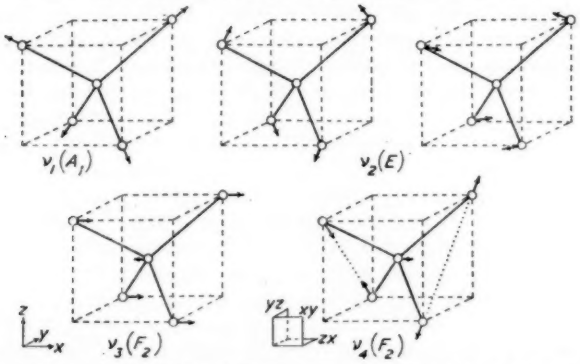
(3) The triply degenerate ν_3 mode occurs in the Raman spectrum [5] as a doublet at 984, 1016 cm.$^{-1}$. The structure of the band is more complex in the infrared region and appears to have about six incompletely resolved components. Increase in the ^{10}B : ^{11}B ratio decreases the absorption near 1038 and 1063 cm.$^{-1}$ and increases it near 1135 and

[4] Hoard and Blair, *J. Amer. Chem. Soc.*, 1935, **57**, 1985.
[5] Goubeau and Bues, *Z. anorg. Chem.*, 1952, **268**, 221.

1158 cm.$^{-1}$. Some of the structure is therefore due to isotope doubling. Superimposed on this is the effect of the crystal field in removing the vibrational degeneracy so that a total of six components is expected. It is unlikely that the intensities of the originally degenerate modes will be equal since this depends on the extent of the distortion due to the field in each direction. For this reason it may well prove impossible to increase the resolution within the band or to observe all three modes and their isotopic doublets as individual maxima.

A further complicating factor must be considered, *viz.*, the accidental degeneracy between $2\nu_4$ and ν_3. The values of ν_4 in the Table being used, the calculated values for $2\nu_4$ are 1050 or 1060 and 1072 or 1084 cm.$^{-1}$. There is thus the possibility that some of the structure in the ν_3 band is due to enhanced absorption of the ν_4 overtone. Should these

FIG. 2. *Normal modes of vibration for a tetrahedral ion* MX_4^-.



$\nu_3(F_2)$ is three degenerate modes involving displacements along the x axis or the y axis or the z axis.
$\nu_4(F_2)$ is three degenerate modes involving displacements along diagonals in the yz or the xy or the zx face.

frequencies coincide exactly with any of the three pairs of originally degenerate ν_3 vibrations then there is also the possibility of Fermi resonance since the symmetry class of the upper state of $2\nu_4$ is $(F_2 + A_1 + E)$.

(4) The ν_4 mode, observed at 524 cm.$^{-1}$ in the Raman spectrum,[5] occurs as a doublet in the infrared region. Enrichment in ^{10}B increases the peak height of the high-frequency component and establishes that the doublet arises from an isotope effect. Mixtures of normal and enriched potassium tetrafluoroborate have relative peak heights intermediate between the two extremes shown in Fig. 1. The separation is 11—12 cm.$^{-1}$ (cf. Coté and Thompson,[3] 13 cm.$^{-1}$). The fact that the ratio of peak heights (or band areas) is not 1 : 4 for the normal compound and 9 : 1 for the enriched sample does not conflict with the assignment of the doublet as an isotope effect for, even with a simple compound such as gaseous boron trifluoride, the intensity ratio of doublets in the unenriched compound is not 1 : 4 but is similar to that shown for ν_4 in Fig. 1.

The symmetrical contours of each component of the doublet indicates that there is no removal of vibrational degeneracy for this mode. This is presumably because each of the deformations involves displacements along parallel faces of the circumscribing cube but in diagonally opposite directions so that the x, y, and z components of the crystal field become, in a sense, averaged out. On the other hand, the three ν_3 vibrations can be considered as involving displacement along the x, or the y, or the z direction of the crystal field so that each is affected differently from the other two.

(5) The bands near 1300 cm.$^{-1}$ are assigned as $(\nu_1 + \nu_4)$, the agreement between calculated and observed frequencies being particularly good for the enriched sample:

1303 and 1315 cm.$^{-1}$, compared with the observed 1305 and 1312 cm.$^{-1}$. Enrichment in ^{10}B enhances the peak height of the high-frequency component as expected. The bands near 1650 cm.$^{-1}$ can be assigned to the combination $(\nu_3 + \nu_4)$. Thus, for the enriched sample, the averaged frequency for ν_4 is 535 cm.$^{-1}$; subtraction of this from the frequencies near 1650 gives for the three ν_3 bands 1086, 1115, and 1135 cm.$^{-1}$, which are close to three of the observed ν_3 frequencies. Agreement for the normal sample is less satisfactory because of the poor resolution of the peaks near 1650 cm.$^{-1}$. The weak absorption at about 2340 cm.$^{-1}$ can be assigned either as $2\nu_3$ or as $(\nu_3 + 2\nu_4)$.

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THE UNIVERSITY, NOTTINGHAM. [*Received, June 10th*, 1959.]

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769. *The Stereochemistry of B Subgroup Metals. Part II.*[1] *The Inert Pair.*

By L. E. ORGEL.

The mixing of *s* and *p* orbitals on a central ion in non-cubic environments which lack a centre of symmetry is shown to account for the stereochemical influence of inert pairs of electrons on the chemistry of Tl^+, Pb^{++}, and related ions.

MANY B subgroup metals exhibit a stable valency two smaller than the group valency. This tendency is most pronounced for thallium, lead, and bismuth and is also important for many lighter elements such as tin and antimony. The stereochemistry of molecules and solids containing ions in these unusual valencies is very often complicated.

The free ions corresponding to the lower valencies all have electron configurations consisting of closed shells followed by a pair of *s* electrons; 6*s* for Tl^+, Pb^{++}, and Bi^{+++}; 5*s* for In^+, Sn^{++}, and Sb^{+++}, etc. It is generally recognized that the unusual stereochemistry of these ions is connected with the pair of electrons outside a closed shell, but various views have been expressed as to the precise way in which the unshared electrons exert their influence. We shall develop the method suggested for d^{10} ions in a previous paper.[1]

We consider first a metal ion with an *s* electron pair at the centre of an octahedron of anions. A symmetrical displacement of the ligands can only mix the orbital containing the unshared *s* electrons with other *s* or *d* orbitals.* Since these are all energetically very highly excited such mixing is unlikely to be important. A displacement of an antisymmetrical kind, however, can mix the top filled *s* orbital with the *p* orbitals of the same subshell, which are known from spectroscopic evidence to be separated from the *s* orbital by only 5—6 ev in typical ionic solids.[2] If the *s* and *p* orbitals were initially degenerate the octahedron would be bound to be distorted, but in view of the actual energy separation between *s* and *p* orbitals it is a quantitative matter to decide whether distortion should occur or not.[1]

We make a very rough estimate of the energy contributed by polarization of the cation in a distorted configuration by adopting a point-charge model. Let us suppose that the anions along the *Z* axis of an octahedral complex are displaced a distance *z* in the same direction. The polarization energy is readily shown to be † $E_p = z^2(8\alpha Q^2/R^6) = \gamma_z{}^2$ where

* This is an example of a very general quantum-mechanical argument which shows that if a system has a centre of symmetry, *g* and *u* states, that is even and odd states, can be mixed by an antisymmetric perturbation while two even or two odd states can be mixed by a symmetric perturbation.

† The field acting on the central ion is $Q\{[1/(R+z)^2] - [1/(R-z)^2]\}$, of which the most important term is $4zQ/R^3$. The polarization energy is $\frac{1}{2}\alpha(4zQ/R^3)^2$.

[1] Orgel, *J.*, 1958, 4186.

[2] Jørgensen, to be submitted for publication.

α is the polarizability of the cation, Q is the charge on the anion and R is the interionic distance.

Ions with an inert s electron pair are undoubtedly much more polarizable than ions of similar atomic number but with filled shells. Experimental values do not seem to be available, but Pauling has calculated the polarizabilities of Al^+ and Si^{++} to be $41{\cdot}2 \times 10^{-25}$ and $20{\cdot}6 \times 10^{-25}$ cm.^{3} compared with values of $1{\cdot}79 \times 10^{-25}$ and $0{\cdot}94 \times 10^{-25}$ cm.^{3} for Na^+

TABLE 1. *Values of γ for various choices of α, R, and z.*

α	$R = 2$ Å; $z = 1$	$R = 2$ Å; $z = 2$	$R = 3$ Å; $z = 1$	$R = 3$ Å; $z = 2$
100×10^{-25}	$2{\cdot}875 \times 10^5$	$11{\cdot}50 \times 10^5$	$0{\cdot}25 \times 10^5$	$1{\cdot}01 \times 10^5$
500×10^{-25}	$14{\cdot}37 \times 10^5$	$57{\cdot}50 \times 10^5$	$1{\cdot}26 \times 10^5$	$5{\cdot}05 \times 10^5$

and Mg^{++}. The polarizabilities of Cs^+, Ba^{++}, and La^{+++} are $25{\cdot}2 \times 10^{-25}$, $15{\cdot}5 \times 10^{-25}$, and $10{\cdot}4 \times 10^{-25}$ cm.^{3}, respectively,[3] suggesting that the polarizabilities of Tl^+, Pb^{++}, and Sb^{+++} are in the range from 100×10^{-25} to 500×10^{-25}. In Table 1 we have collected some typical values for γ, reasonable values for R and α being assumed. It will be seen that γ is of the order of 10^5 dyne/cm., which is just the order of the force constants in

FIG. 1. *The structures obtained by the distortion of a regular octahedron along* (a) *a fourfold axis,* (b) *a twofold axis,* (c) *a threefold axis.*

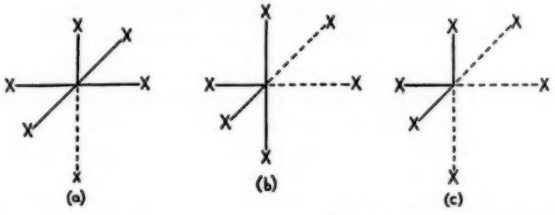


FIG. 2. *The structure obtained by distorting a cube about a fourfold axis.*

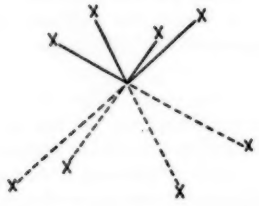
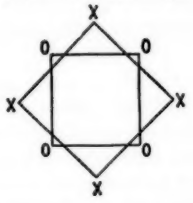


FIG. 3. *The structure obtained by distorting a square antiprism about a fourfold axis. The* 0's *represent atoms above the plane and the* ×'s *atoms below the plane.*



typical oxides.[4] Thus, if we compare a stable regular octahedrally co-ordinated oxide of an A subgroup element with a corresponding B subgroup oxide, the difference in polarizability due to the inert pair is sufficient to loosen the metal ion at the centre of the octahedron or even to lead to instability.

It should be noted that the stabilization energies increase rapidly as R decreases so that in so far as their origin is electrostatic these distortions can be expected to be most evident in oxides and fluorides and less so in sulphides, chlorides, etc.* This is exactly the opposite conclusion to that which is reached if covalent influences are supposed to be dominant. We shall see that in fact this distance effect does seem to be important in some, if not all, classes of compound, *e.g.*, SnS and PbO are strongly distorted while PbS, PbSe, and PbTe, although presumably more covalent, have the sodium chloride structure.

* This assumes that the restoring force constants k are less sensitive than is γ to changes in R.

[3] Landolt-Börnstein, "Zahlenwerte und Functionen," Vol. I, Part I, Springer, Berlin, 1950.
[4] Herzberg, "Infra-red and Raman Spectra," 1945, van Nostrand, New York.

We now consider the environments of metal ions which can be derived from regular co-ordination if antisymmetric distortions are present. We start with a regular octahedron and consider the displacements which are symmetric about four-, two-, and three-fold axes, respectively. They lead to the configurations shown in Fig. 1. Each of these is encountered among the complexes and binary compounds of many ions with s^2 ground states. Starting from a cubic environment there are again three simple types of distortion, as shown in Fig. 2. Only the first is easily recognized, for example among the compounds of the larger ions, Pb^{++} and Bi^{+++}. Finally starting with a square antiprism the most symmetrical distortion is to the configuration shown in Fig. 3 and again is found most often for the larger ions, Pb^{++} and Bi^{+++}. We must emphasize that structures which are not closely related to cubic co-ordination may occur when the stereochemical influence of the inert pair is great, and that they should all lack even an approximate centre of symmetry.

Structural Evidence.—We have shown that ions with an s^2 outer electron configuration should often occur in environments lacking a centre of symmetry. An interesting comparison is thus possible between compounds of B subgroup elements for which a sodium chloride or cæsium iodide structure might be expected if distortions were absent. We have already seen that mercuric sulphide in the form of cinnabar can be considered to have a strongly distorted sodium chloride structure which nearly retains its centre of symmetry and that mercuric oxide also has a centro-symmetric structure based on a very distorted octahedral co-ordination.[1] Now stannous sulphide also has a deformed sodium chloride structure but one pair of opposite bonds have lengths of 2·62 Å and 3·39 Å, respectively, while the remaining four bonds occur in two opposed pairs each consisting of one short (2·68 Å) and one long (3·27 Å) bond.[5] Stannous and plumbous oxide are dimorphic, but the form whose structure is known most certainly can be considered to have a very strongly distorted cæsium iodide structure while the other form has a very unsymmetrical octahedral environment about the metal atom.[5] We have noted that PbS, PbSe, PbTe, and SnTe, which are presumably more covalent than the compounds discussed so far, all have undistorted sodium chloride structures.[5]

We can select only a few compounds containing s^2 ions from the many complex halides, oxides, and sulphides which have been studied. Many more are catalogued.[5] The five-co-ordinated structure (Fig. 1) occurs for example in K_2SbF_5,[6] and $KSbF_4$;[7] the four-co-ordinated structure (Fig. 1) in the $Sb_8O_8(OH)_4^{4+}$ ion [8] and the three-co-ordinated structure (Fig. 1) for example in GeO, As_2O_3, and Sb_2O_3.[5] The four-co-ordinated structure shown in Fig. 1a occurs in SnO,[5] PbO,[5] and $BiSbO_4$.[9] The square antiprism (Fig. 3) occurs in $Pb_2Cu(OH)_4Cl_2$.[10] The Cu^{++} ion shows the usual Jahn–Teller distorted 4 + 2 co-ordination but the lead atom is surrounded by four close oxygen atoms on a square, and four more-distant chloride ions completing an antiprism.

The distribution of more-distant neighbours in these compounds is interesting. When the distortion is along the four-fold axis of a cube or the three-fold axis of an octahedron both the short and the long bonds can often be recognized, for example in PbO, GeO, and Sb_2O_3. When, however, the distortion is along the four-fold axis there is usually no unique sixth group completing the octahedron. The case of distortion along a two-fold axis is intermediate. This can be most easily understood by considering the charge density distribution of the unshared pair after polarization. In the case of five-fold co-ordination these electrons are in an orbital pointing directly at the sixth position so an arrangement such as that in Fig. 4 is preferred. However, in the case of three close groups the unshared pair points along a three-fold axis of the original octahedron so that the remaining vertices of that octahedron are still the most favourable positions for weak attachments. The

[5] Landolt-Börnstein, " Zahlenwerte und Functionen," Vol. I, Part IV, Springer, Berlin, 1950.
[6] Byström and Wilhelmi, *Arkiv Kemi*, 1951, **3**, 461.
[7] Byström, Backlund, and Wilhelmi, *Arkiv Kemi*, 1952, **4**, 175.
[8] Edstrand, *Arkiv Kemi*, 1955, **8**, 257.
[9] Aurivillius, *Arkiv Kemi*, 1951, **3**, 153.
[10] Byström and Wilhelmi, *Arkiv Kemi*, 1950, **2**, 397.

same argument shows that four next-nearest neighbours should be recognizable in the case of displacement along the four-fold axis of a cube or square antiprism.

The occurrence of phase transitions between structures of cubic symmetry and distorted structures has been recognized among the oxides with the perovskite structure containing the Pb^{++} ion. Megaw [11] has shown that at least in a few cases the distortions must in large measure be attributed to the stereochemical irregularities of the Pb^{++} ion.

The Polarizability of Undistorted Structures and Ferroelectricity.—We have suggested that the possibility of *s–p* mixing causes a tendency to instability to antisymmetric distortions in a cubically co-ordinated ion with an unshared *s* electron pair. This leads to the prediction that even if the cubic structure is stable it should be particularly susceptible to atom polarization by a static electric field, since the restoring force opposing ionic

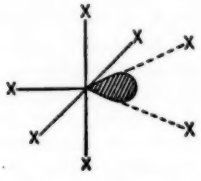


FIG. 4. *An electrostatically favourable arrangement of next-nearest neighbours about a five co-ordinated metal ion.*

displacements should be reduced. In fact, thallium chloride and bromide, which have the cæsium iodide structure, have extremely large dielectric constants—much larger than can be accounted for even when the large electron polarizability of the Tl^+ ion is allowed for. This situation can be compared with that in titanium dioxide, which for different reasons is very unstable to antisymmetric displacement of the Ti^{4+} ions and so has a very large dielectric constant.[12]

In other compounds of Tl^+, Pb^{++}, etc., the distortions accompanying *s–p* mixing may be responsible for the often large dielectric constants. On the other hand, mercuric compounds based on octahedral co-ordination should not show this anomalous behaviour since the distortions characteristic of these ions do not lead to net dipole moments and indeed their polarizabilities are not abnormal. This suggests that among oxides, etc., ferroelectric compounds will be found most often if metal ions are present which are stabilized by antisymmetric distortions.

Relation to Previous Theories of Bond Type.—The account of the stereochemical influence of the inert pair which we have obtained by considering the mixing of *s–p* orbitals is closely related to the conventional electrostatic theory.[13] It amplifies this latter theory by:

(*a*) Giving a very simple explanation of the differences between the deviations from ionic packing found with d^{10} and $d^{10}s^2$ ions.

(*b*) Showing that the unusual stereochemical properties observed in certain discrete molecules and complex ions represent the extreme examples of a much more general phenomenon. The occurrence of minor distortions from cubic symmetry, for example in stannous compounds, and the appearance of a high static dielectric constant, for example in thallium chloride, do not seem to have been recognized as consequences of the " stereochemical properties " of the inert pair.

(*c*) Providing the basis for calculations of the paramagnetic contribution to the susceptibility and the chemical shifts observed in the nuclear magnetic resonance spectra of Tl^+, Pb^{++}, compounds, etc.[14]

It is more difficult to assess the relevance of this approach to the nature of the bonding in crystals containing Pb^{++} ions, etc. Undoubtedly the metal ion in a distorted complex has an electron distribution which is far from spherically symmetrical. The electron

[11] Megaw, " Ferroelectricity in Crystals," Methuen, London, 1957.
[12] Orgel, *Discuss. Faraday Soc.*, 1958, No. 26, 138.
[13] Wells, " Structural Inorganic Chemistry," 2nd edn., Oxford University Press, 1951.
[14] Orgel, *Mol. Physics*, 1958, **1**, 322.

affinity is consequently much greater in the direction of the shorter bonds than it would be in a symmetrical environment and these bonds are therefore stronger, and in this sense more covalent. However, as in transition-metal chemistry, the stereochemistry is determined in large measure by the electronic structure of the ground and the lowest excited states of the free ion and not by the tendency of the ligands to form covalent bonds. It is for this reason that oxides and fluorides show a greater tendency to distortion (and hence possibly a greater deviation from ionic bonding) than sulphides and other halides.

The electrostatic crystal-field theory and the molecular-orbital theory lead to similar qualitative conclusions in problems of transition-metal stereochemistry.[15,16] An extension of these arguments to the stereochemistry of the inert pair is quite straightforward, and if we had been interested in molecules such as Ph_2TeCl_2 we could have used the molecular-orbital approach instead of an electrostatic theory. For example, in a covalent tetrahedral molecule such as silicon tetrachloride the main bonding is due to the combination of *s* and *p* orbitals on the metal with orbitals on the chlorine atoms. This gives rise to four bonding and four antibonding orbitals, the former of which are filled and the latter empty. In a molecule such as sulphur tetrachloride the two *s* electrons would have to go into a strongly antibonding orbital if the molecule were to remain tetrahedral. However, a distortion from tetrahedral symmetry allows the use of *s*, *p*, and *d* orbitals for bonding and leaves an almost non-bonding *sp* hybrid orbital to accommodate the extra electrons. If the gain in bonding energy compensates for the promotion energy from *s* to *p* and *d* orbitals then the regular tetrahedral molecule must be unstable. This shows very clearly why the extent of distortion depends on the *s*–*p* separation.

Considerations of this sort lead to the same qualitative conclusions about stereochemistry as the electrostatic arguments advanced in greater detail. They are capable of considerable elaboration to take into account π bonding, the use of *d* orbitals in bonding, etc. It follows, therefore, that stereochemistry alone gives little information about the covalent or ionic character of the bonding.

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, January 23rd*, 1959.]

[15] Ballhausen and Moffitt, *Ann. Rev. Phys. Chem.*, 1956, **7**, 107.
[16] Griffith and Orgel, *Quart. Rev.*, 1957, **11**, 318.

770. *Acylarylnitrosamines. Part VIII.*[1] *Reactions of Some o-Methoxy-nitrosoacetamido-compounds.*

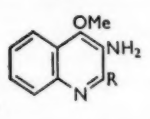
By YUSUF AHMAD and D. H. HEY.

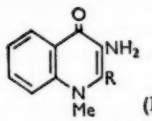
2-Methoxy-1- and 1-methoxy-2-nitrosoacetamidonaphthalene react with benzene in the normal manner to give 2-methoxy-1- and 1-methoxy-2-phenylnaphthalene respectively. In similar manner, 4-methoxy-3-nitrosoacetamidoquinoline gives 4-methoxy-3-phenylquinoline. Freshly prepared nitrosyl chloride is essential for the preparation of the nitroso-compounds. The presence of a methoxyl group in the *ortho*-position with reference to an acetamido-group does not prevent nitrosation, and such nitrosoacetamido-compounds display normal properties.

IN a previous communication [1] it was reported that, contrary to the abnormal behaviour observed in a few quinoline compounds,[2] the 3-amino-group in pyridine, with a methoxyl group in the 2-, 4-, or 6-position with reference to it, behaves normally in reactions which result in its replacement by a phenyl group. It thus seemed likely that the abnormal behaviour reported for 3-amino-4-methoxy-quinoline (I; R = H) and -quinaldine (I; R = Me) was not associated with the difference in the structure of the isomeric *O*- and *N*-methyl derivatives (I) and (II). Nor could such behaviour be entirely attributed to the

[1] Part VII, Ahmad and Hey, *J.*, 1954, 4516.
[2] Adams and Hey, *J.*, 1951, 1521.

proximity of the methoxyl group in the benzenoid structure (I), because it is known that *o*-anisidine reacts normally (as the diazonium salt) with pyridine to give a mixture of *o*-methoxyphenylpyridines [3] in 50% yield. On the other hand, it has been reported [4] that


(I)


(II)

derivatives of 5-amino-6-methoxyquinoline failed to react with pyridine to give pyridyl derivatives. Attention was therefore directed to similar reactions in the naphthalene series with derivatives containing an amino-group in an *ortho*-position with reference to a methoxyl group (*i.e.*, the carbocyclic analogues of the above quinoline compounds). Methoxynaphthylamines in which the amino- and the methoxyl group occur in separate rings have been successfully subjected to reactions which result in replacement of the amino-group by the phenyl group,[5] but similar reactions with naphthalene derivatives in which the methoxyl and amino-groups occur at adjacent positions in the same ring have not hitherto been investigated.

1-Acetamido-2-methoxynaphthalene underwent normal nitrosation and, when the *N*-nitroso-derivative was heated in benzene solution, it gave 2-methoxy-1-phenylnaphthalene in low yield. In similar manner nitrosation of 2-acetamido-1-methoxynaphthalene gave the nitroso-compound, which decomposed normally in benzene to give 1-methoxy-2-phenylnaphthalene; some 1-methoxynaphthalene was also isolated from this reaction. In the nitrosation of both acetamidomethoxynaphthalenes it was observed that only freshly prepared nitrosyl chloride in solution in acetic anhydride was capable of effecting the reaction. If an old solution was used the unchanged acetamido-compounds were recovered or unidentified products were formed.

These observations made it necessary to reinvestigate the nitrosation of 4-methoxy-3-acetamidoquinoline, and it was found that when freshly prepared nitrosyl chloride in acetic anhydride was used 4-methoxy-3-*N*-nitrosoacetamidoquinoline was obtained as viscous yellow oil. The nitroso-compound exhibited normal chemical properties, and it decomposed in warm benzene with evolution of nitrogen to give 4-methoxy-3-phenylquinoline in low yield.

In another investigation,[6] 8-acetamido-7-methoxyisoquinoline has also been converted into a normal nitroso-compound which decomposed in benzene to give 7-methoxy-8-phenylisoquinoline in the usual manner. It may thus be concluded that the presence of a methoxyl group in the *ortho*-position with reference to an amino-group, in both carbocyclic and heterocyclic compounds, does not prevent the nitrosation of the acetyl derivatives, and that such nitroso-compounds display their normal decomposition reactions.

Experimental

Light petroleum had b. p. 40—60°. The alumina used for chromatography was " Activated Alumina Type ' H ' " supplied by Peter Spence & Sons, Ltd.

2-*Methoxy*-1-N-*nitrosoacetamidonaphthalene*.—A 25% solution of nitrosyl chloride in acetic anhydride (15 c.c.) was added dropwise to a well-stirred mixture of 1-acetamido-2-methoxynaphthalene [7] (5·0 g.) in glacial acetic acid (20 c.c.) and acetic anhydride (15 c.c.) containing fused potassium acetate (15·0 g.) and phosphoric oxide (0·5 g.) at 0°. Stirring was continued for 20 min. after the addition, and the thin yellow paste was then poured on crushed ice and aqueous sodium hydroxide (40 g. in about 100 c.c.) with vigorous stirring. The nitroso-compound separated as an orange oil, which solidified (5·25 g. after being dried overnight at 0—2° *in vacuo*

[3] Haworth, Heilbron, and Hey, *J.*, 1940, 358.
[4] Coates, Cook, Heilbron, Hey, Lambert, and Lewis, *J.*, 1943, 401.
[5] Hey and Lawton, *J.*, 1940, 374, 384.
[6] Ahmad and Hey, unpublished work.
[7] Davis, *Chem. News*, 1896, **74**, 302.

over potassium hydroxide). A portion was purified by dissolution in cold dry ether (charcoal) and removal of ether *in vacuo* under moisture-proof conditions. 2-*Methoxy*-1-N-*nitrosoacetamidonaphthalene* was obtained as deep yellow powder, shrinking to a dark red melt with evolution of gas at 86—88° (Found: C, 63·6; H, 5·0. $C_{13}H_{12}O_3N_2$ requires C, 63·9; H, 4·9%). The nitroso-compound is fairly stable at room temperature.

2-*Methoxy*-1-*phenylnaphthalene*.—The above nitroso-compound (4·25 g.) was dissolved in dry " AnalaR " benzene (150 c.c.), filtered, and then heated under gentle reflux for 24 hr. under moisture-proof conditions. Nitrogen was evolved and the solution became dark red. After removal of solvent the dark red, tarry residue was dissolved in the minimum quantity of benzene and passed down a column of alumina, which was eluted first with light petroleum and then with light petroleum–benzene (1 : 1). Removal of solvent left a light yellow oil, which solidified to a very low-melting solid (0·5 g.), the *picrate* of which separated from benzene in deep red prisms, m. p. 151—152° (Found: C, 60·1; H, 3·7. $C_{17}H_{14}O,C_6H_3O_7N_3$ requires C, 59·6; H, 3·6%).

2-*Acetamido*-1-*methoxynaphthalene*.—Aceto-α-naphthalide was nitrated by Hodgson and Kilner's method,[8] and the resulting mixture of nitro-compounds was hydrolysed to 2- and 4-nitro-1-naphthol from which the former was removed by distillation with steam. The 2-nitro-1-naphthol was converted into 1-methoxy-2-nitronaphthalene by a method similar to that of Jones and Sleight,[9] by treating dry sodium 2-nitro-1-naphthoxide with methyl sulphate and toluene for 1 hr. at 110—120°. A solution of 1-methoxy-2-nitronaphthalene (7 g.) in methanol (170 c.c.) containing Raney nickel (7 g.) was shaken with hydrogen at room temperature and atmospheric pressure. The theoretical volume of hydrogen was rapidly taken up and the solution was filtered. Excess of solvent was removed and the cooled solution was poured into ice-cold water. The 1-methoxy-2-naphthylamine, which separated in quantitative yield (needles from dilute methanol; m. p. 48—49° [10]), was acetylated with acetic anhydride containing 3—4 drops of perchloric acid. The mixture was poured on ice, and the acetyl derivative was collected, washed with dilute sodium hydroxide and water, and dried (yield quantitative). 2-Acetamido-1-methoxynaphthalene crystallised from dilute methanol (charcoal) in pinkish-white plates, m. p. 131—132°.[10]

1-*Methoxy*-2-N-*nitrosoacetamidonaphthalene*.—Nitrosyl chloride in acetic anhydride (15% solution; 36 c.c.) was added dropwise to a stirred mixture of 2-acetamido-1-methoxynaphthalene (4 g.), fused potassium acetate (6 g.), glacial acetic acid (15 c.c.), acetic anhydride (10 c.c.), and phosphoric oxide (0·5 g.) at 0—5°. After 25 min. the mixture was poured on crushed ice containing sufficient aqueous sodium carbonate to make the mixture slightly alkaline. An orange-yellow oil separated, which solidified. It was filtered off quickly, washed with ice-cold water, and dried *in vacuo* over potassium hydroxide (yield almost quantitative). A small portion, purified by dissolution in cold dry ether (charcoal), gave 1-*methoxy*-2-N-*nitrosoacetamidonaphthalene* as a pale yellow amorphous powder, m. p. 73° (decomp.) (Found: C, 64·2; H, 5·1. $C_{13}H_{12}O_3N_2$ requires C, 63·9; H, 4·9%). The temperature during all these operations was kept below 5°.

1-*Methoxy*-2-*phenylnaphthalene*.—A solution of 1-methoxy-2-*N*-nitrosoacetamidonaphthalene (4 g.) in dry " AnalaR " benzene (100 c.c.) was heated under gentle reflux for 24 hr. Nitrogen was evolved and the yellow solution became dark red. After removal of some of the solvent the solution was passed down a column of alumina, which was eluted with light petroleum. Removal of solvent gave a colourless oil, which solidified. Crystallisation from dry ether gave 1-*methoxy*-2-*phenylnaphthalene* (0·3 g.) in needles, m. p. 56—57° (Found: C, 86·8; H, 6·15. $C_{17}H_{14}O$ requires C, 87·1; H, 6·0%). Further elution of the column with benzene gave 1-methoxynaphthalene as a pale yellow oil (0·25 g.), which did not solidify. It gave an orange-red *picrate*, m. p. 127·5—128·5° (Found: C, 52·7; H, 3·55. $C_{11}H_{10}O,C_6H_3O_7N_3$ requires C, 52·7; H, 3·4%). The m. p. was not depressed on admixture with an authentic specimen prepared from 1-methoxynaphthalene.

3-*Acetamido*-4-*methoxyquinoline*.—3-Amino-4-methoxyquinoline was obtained as described by Adams and Hey,[2] the only modification made in the procedure being the use of 5% palladium–carbon instead of platinum for the reduction of the nitro-group. For acetylation of the amine in the cold with acetic anhydride perchloric acid was added in place of sulphuric acid

[8] Hodgson and Kilner, *J.*, 1924, 808.
[9] Jones and Sleight, *J.*, 1954, 1780.
[10] Noelting, Grandmougin, and Freimann, *Ber.*, 1909, **42**, 1384.

as catalyst. The acetyl derivative crystallised from acetone (charcoal) in light yellow needles, m. p. 74°. When this was heated for 24 hr. under reflux with benzene (in which it was only sparingly soluble in cold) and the hot solution was allowed to cool slowly, 3-acetamido-4-methoxyquinoline separated quantitatively as colourless, long prismatic needles and the m. p. rose to 76°. No trace of the high-melting quinolone was isolated. The m. p. rose to 111—112° when the crystals were dried over potassium hydroxide *in vacuo* for a few days. Adams and Hey [2] quote m. p. 74° for the hemihydrate and m. p. 105° for the anhydrous compound.

4-Methoxy-3-N-nitrosoacetamidoquinoline.—A freshly prepared solution (25%; 8 c.c.) of nitrosyl chloride in acetic anhydride was added dropwise to a stirred mixture of 3-acetamido-4-methoxyquinoline (2·5 g.) fused potassium acetate (7·5 g.), glacial acetic acid (10 c.c.), acetic anhydride (7·5 c.c.), and phosphoric oxide (0·25 g.) at 0°. Stirring was continued for 15 min. and the thin yellow paste was poured on crushed ice and aqueous sodium hydroxide (20 g. in 50 c.c.). A thick yellow oil separated which failed to solidify. The oil was removed and the aqueous layer was extracted with " AnalaR " benzene. The oil, except for a small portion, was added to the benzene extract, and the yellow benzene solution was dried ($NaSO_4$) overnight below 10°. Purification of a small portion by dissolution in cold dry ether (charcoal) gave a pale yellow viscous oil, which was dried *in vacuo* over potassium hydroxide at 0° for 24 hr. (Found: C, 56·6; H, 5·0. $C_{12}H_{11}O_3N_3,\frac{1}{2}H_2O$ requires C, 56·7; H, 4·7%). The nitroso-compound, on being warmed above 60° or on storage at room temperature for a few days, darkened and underwent decomposition with evolution of gas.

4-Methoxy-3-phenylquinoline.—The dried benzene solution of the above nitroso-compound was heated under reflux for 24 hr. Nitrogen was evolved and the solution became dark red. Benzene was removed under reduced pressure and the dark red residue was digested with dry ether. The ether extract was filtered and evaporated. The residue in the minimum quantity of benzene was passed down a column of alumina, which was eluted with light petroleum–benzene (1 : 1). On removal of solvents a colourless oil was obtained, which solidified (0·25 g.). Its picrate separated from benzene in bright yellow needles m. p. 156—158°, alone or on admixture with the picrate of 4-methoxy-3-phenylquinoline.[2] A marked depression was recorded on admixture with the picrate of 1-methyl-3-phenyl-4-quinolone.[2]

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771. *Determination of the Ionization Constant of Hydrocyanic Acid at 25° by a Spectrophotometric Indicator Method.*

By K. P. ANG.

Spectrophotometric measurements of the spectrum of *m*-bromophenol in buffers of hydrocyanic acid and sodium cyanide have been used to give pK 9·21$_6$ for hydrocyanic acid. *m*-Bromophenol has pK 9·00$_4$.

WHEN the spectrophotometric method is used to determine the ionization constant of a weak acid, *e.g.*, by measurement of the absorption spectrum of *p*-nitrophenol in phosphate buffers,[1] the buffer constituents are necessarily in comparatively high concentration but are optically transparent (or at least have small optical densities); it is the weak acid added at low concentration to the buffer which affords the optical absorption whose change with pH gives the ionization constant of the acid. The method can, however, be used in reverse if the ionization constant of the " coloured " acid is known, to give the ionization constant of the acid in the buffer mixture; it now becomes essentially a quantitative indicator method extended to the ultraviolet region of the spectrum.

[1] Robinson and Biggs, *Trans. Faraday Soc.*, 1955, **51**, 901.

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The equilibria in a buffer solution containing a " coloured " acid are governed by two equations:

$$pK_R = pH - \log([Salt]/[Acid]) - \log \gamma_R \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where K_R is the ionization constant of the buffer acid, γ_R the activity coefficient of its anion and the [Salt]/[Acid] ratio is corrected for hydrogen-ion concentration if the buffer acid is only moderately weak and for the hydroxyl-ion concentration if it is very weak. Eqn. (2) relates the ionization constant of the " coloured " acid to the optical densities of its solution:

$$pK = pH - \log(D_1 - D)/(D - D_2) - \log \gamma_B \quad . \quad . \quad . \quad . \quad (2)$$

where γ_B is the activity coefficient of its anion, D_1 is the optical density in a solution of low pH where all the " coloured " acid is present in the undissociated form, D_2 that in a solution of high pH containing only the dissociated species, and D that in the buffer solution. If the anion of the " coloured " acid and that of the buffer acid are of the same valency type, a good approximation is:

$$pK = pK_R + \log([Salt]/[Acid]) - \log(D_1 - D)/(D - D_2) \quad . \quad . \quad . \quad (3)$$

Thus either pK or pK_R can be determined if the other is known.

In previous work [2] on *p*-iodobenzoic acid it was noted that the apparent pK values from measurements in formate and succinate buffers differed by some 0·02 unit. This was

TABLE 1.

Barbituric acid, 9·32 × 10^{-6}M; wavelength, 258 mμ; 4 cm. cells; temperature, 25°; D_1 (in M-HCl) 0·014; D_2 (in 0·001M-NaOH) 0·785.

Molality of acid	D	log ([Salt]/[Acid])	log $(D_1 - D)/(D - D_2)$	pK
Formic acid, 1 mol.	Sodium formate, 1·923 mol.			
0·001733	0·427	0·321	0·062	4·011
0·003466	0·423	0·304	0·053	4·003
Formic acid, 1 mol.	Sodium formate, 1·504 mol.			
0·001989	0·375	0·222	−0·055	4·029
0·003978	0·364	0·201	−0·080	4·033
Formic acid, 1 mol.	Sodium formate, 1 mol.			
0·002533	0·311	0·059	−0·203	4·014
0·005066	0·300	0·033	−0·229	4·014
				Mean 4·017
Succinic acid, 1 mol.	Sodium hydrogen succinate, 0·5 mol.		Sodium chloride, 1 mol.	
0·02	0·343	−0·315	−0·128	4·020
0·03	0·337	−0·321	−0·142	4·028
0·04	0·338	−0·326	−0·140	4·021
0·05	0·339	−0·328	−0·138	4·017
Succinic acid, 1 mol.	Sodium hydrogen succinate, 0·5 mol.		Sodium chloride, 0·5 mol.	
0·02	0·340	−0·318	−0·135	4·024
0·03	0·343	−0·322	−0·128	4·013
0·04	0·339	−0·324	−0·137	4·020
0·05	0·340	−0·327	−0·135	4·015
Succinic acid, 1 mol.	Sodium hydrogen succinate, 0·5 mol.			
0·02	0·343	−0·321	−0·128	4·014
0·03	0·343	−0·323	−0·128	4·012
0·04	0·338	−0·322	−0·140	4·025
0·05	0·343	−0·326	−0·128	4·009
				Mean 4·018

not a favourable example to which to apply the method because the separation between the spectra of the undissociated and the dissociated form was not wide, and to resolve doubts about the use of these buffers, the method has now been checked in the more favourable case of barbituric acid, with the results given in Table 1. As the mean values

[2] Robinson and Ang, *J.*, 1959, 2314.

from the formate and the succinate buffer are in good agreement, it is now believed that the difficulties encountered with iodobenzoic acid were due to the limited accuracy which could be achieved in this unfavourable case.

The mean of the 18 determinations is $4{\cdot}01_8$, but a higher value, $4{\cdot}03_5$, has been derived from measurements in succinate buffers.[3]

Having demonstrated that the formate and succinate buffers give the same result, the reverse determination can be illustrated with hydrocyanic acid. In this method the "coloured" acid should have about the same pK; *m*-bromophenol was chosen. In Table 2 are recorded the data necessary for the determination of its pK in borax buffers for which pH values have already been reported;[4] γ_B in equation (2) was calculated as before[3] by the equation $-\log \gamma_B = 0{\cdot}5092\sqrt{I}/(1 + \sqrt{1}) - 0{\cdot}2I$. A small correction[5]

TABLE 2. *Ionization constant of* m-*bromophenol.*

m-Bromophenol, $2{\cdot}28 \times 10^{-4}$M; wavelength, 294 m$\mu$; 1 cm. cells; temperature, 25°; D_1 (in 0·01M-HCl) 0·019; D_2 (in 0·01M-NaOH) 0·715.

Molality of borax	D	$\log (D_1 - D)/(D - D_2)$	pH	$-\log \gamma_B$	pK
0·010	0·456	0·227	9·177	0·059	9·009
0·025	0·464	0·249	9·172	0·083	9·006
0·050	0·480	0·293	9·196	0·102	9·005

Corrected pK = 9·004.

was applied to allow for the effect of bromophenol on the pH of the buffer mixture, giving pK $9{\cdot}00_4$. From this, the extent of dissociation of the bromophenol in hydrocyanic acid–sodium cyanide buffers was measured as shown in Table 3. Application of equation (3) gave

TABLE 3. *Ionization constant of hydrocyanic acid.*

m-Bromophenol, $2{\cdot}28 \times 10^{-4}$M; wavelength, 294 m$\mu$; 1 cm. cells; temperature, 25°.

Molality of HCN	D	$\log$ ([Salt]/[Acid])	$\log (D_1 - D)/(D - D_2)$	pK
HCN, 1 mol. NaCN, 0·8411 mol.				
0·005435	0·421	−0·077	0·136	9·217
0·01087	0·421	−0·076	0·136	9·216
0·02174	0·418	−0·076	0·128	9·208
HCN, 1 mol. NaCN, 1·032 mol.				
0·004919	0·456	0·011	0·227	9·220
0·009838	0·455	0·012	0·224	9·216
0·01968	0·456	0·013	0·227	9·218
			Mean	9·216

pK $9{\cdot}21_6$ for hydrocyanic acid, a value considerably lower than many which have been reported[6] based on potentiometric titration: what have been recorded are probably "concentration" ionization constants with pK 9·3; any correction to give thermodynamic ionization constants would raise pK to about 9·4. The value now reported depends on the well-substantiated pH values of borax solutions, and the only uncertainty is in the value of γ_B used in calculating the pK of *m*-bromophenol; arbitrary to some extent as this is, it is not believed that it can influence the pK of hydrocyanic acid by more than $\pm 0{\cdot}01$.

Experimental.—Measurements of the optical density of barbituric acid solutions were made with a Uvispek instrument in an air-conditioned room at 25°; other measurements were made with a Beckman Model DU instrument at 25°.

Barbituric acid was purified by three recrystallisations from water (m. p. 250°), and *m*-bromophenol by distillation under reduced pressure (b. p. 86°/0·5 mm.); samples taken before

[3] Biggs, *J.*, 1956, 2485.
[4] Manov, DeLollis, Lindvall, and Acree, *J. Res. Nat. Bur. Stand.*, 1946, **36**, 543.
[5] Robinson and Kiang, *Trans. Faraday Soc.*, 1955, **51**, 1398.
[6] Britton and Robinson, *J.*, 1931, 458; *Trans. Faraday Soc.*, 1932, **28**, 531; Britton and Dodd, *J.*, 1931, 2332.

and after distillation gave the same pK values, but those recorded in Table 2 refer to a distilled sample.

Hydrocyanic acid was prepared by slow distillation of a potassium cyanide solution acidified with dilute sulphuric acid, and buffer mixtures were prepared from it by partial neutralisation of the acid with carbonate-free sodium hydroxide. The concentration of the acid, determined by silver nitrate titration,[7] was checked at the end of the experiment and no change was detected. Measurements made on potassium cyanide solutions partially neutralised with hydrochloric acid gave the same pK value.

I thank Professor R. A. Robinson for discussions.

UNIVERSITY OF MALAYA, SINGAPORE. [*Received, June 1st,* 1959.]

[7] Diehl and Smith, " Quantitative Analysis," Wiley, New York, 1952.

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772. *Reactions of Triethyltin Chloride with Amines.*

By K. K. JOSHI and P. A. H. WYATT.

Vapour-pressure and freezing-point measurements have been made on the binary systems formed by triethyltin chloride, Et_3SnCl, with dimethylamine, diethylamine, and trimethylamine. In all cases a 2 : 1 ($2Et_3SnCl$: 1 amine) compound is formed as a solid (m. p. 14·8°, 0·9°, and 8·3° respectively); this is accompanied, for dimethylamine, by the appearance in the liquid of an absorption band at 300 mμ, whilst the electrical conductance shows that some ionic species must be present. A 1 : 1 compound also exists for Me_2NH (m. p. 14·7°), and is detectable for Et_2NH (m. p. −4·0°) but undetectable for Me_3N. No 1 : 2 compounds are formed. Pyridine probably forms only the 1 : 1 compound.

AMONGST the addition compounds formed from tin(IV) halides and donor compounds, those containing one molecule of tin(IV) halide to two molecules of donor are perhaps the most important and were regarded by Werner and Pfeiffer [1] as indicating a co-ordination number of six for tin. (For recent views see Bannister and Fowles.[2]) Some compounds containing a greater proportion of the donor have been described,[3] and some containing less, principally the 1 : 1 compounds formed by trialkyltinhalides.[4] However, only one case appears to have been recorded of a 2 : 1 compound in these systems, that formed by stannic chloride and anisole, as indicated by the solid–liquid equilibrium studies by Sisler and his co-workers.[5] This compound was highly dissociated in the liquid phase and could be explained by crystal packing. Our present work shows that this 2 : 1 type of compound occurs in triethyltin chloride systems, where it has some significance in the liquid phase.

Compounds of triethyltin chloride and some common amines could not at first be prepared by precipitation from solution, but a freezing-point investigation showed that 2 : 1 and 1 : 1 compounds do exist, melting just below room temperature. In view of the characteristic absorption spectra and conductances observed in the dimethylamine system, it seems that fuller investigations of this kind may prove worthwhile in other tin(IV) systems.

Freezing-point and vapour-pressure measurements are here recorded for the binary systems formed by triethyltin chloride with dimethylamine, diethylamine, trimethylamine, and pyridine. The dimethylamine system has been investigated more fully, as an example, by spectrophotometric and conductance measurements. Supplementary cryoscopic results are also quoted where relevant.

[1] Werner and Pfeiffer, *Z. anorg. Chem.*, 1898, **17**, 82.
[2] Bannister and Fowles, *J.*, 1958, 751.
[3] Trost, *Canad. J. Chem.*, 1952, **30**, 834, 842; Ephraim and Schmidt, *Ber.*, 1909, **42**, 3856.
[4] Kraus and Greer, *J. Amer. Chem. Soc.*, 1923, **45**, 2946, 3078.
[5] Sisler, Wilson, Gibbins, Batey, Pfahler, and Mattair, *J. Amer. Chem. Soc.*, 1948, **70**, 3818.

Experimental

Since it was necessary to protect the tin compounds from hydrolysis, all cells for physical measurements were modified for attachment to a vacuum line. This was of standard design,[6] built in this laboratory under the direction of Dr. R. C. Cass, whom we thank. Freezing-point and vapour-pressure measurements were carried out in a small cryoscope of 5 ml. capacity, similar to that used for sulphuric acid.[7] The contents were stirred with a single-armed magnetic stirrer and temperatures were measured with a calibrated single-junction copper–constantan thermocouple. The cryoscope was surrounded by a glass jacket immersed in a bath at 1·2° below the freezing-point and solidification was induced usually by touching the supercooled cell with solid carbon dioxide. Since great accuracy was not sought, the temperature was only recorded to $\pm 0{\cdot}1°$ and no supercooling corrections were made. This cryoscope could also be connected through a tap to a mercury manometer for the vapour-pressure measurements. (These are recorded for 20°, but vapour pressures were also determined at the freezing-points of the mixtures, since the quantity of amine in the vapour phase often necessitated a significant correction to the liquid composition, which was different for the freezing-point and 20°.) In carrying out a series of measurements, successive quantities of amine were condensed on a weighed quantity of the tin compound in the evacuated cryoscope, either from a calibrated gas reservoir or, for liquids, from a graduated glass tube of narrow bore sealed to the vacuum line. With pyridine a slight modification was made so that all parts of the cryoscope could be submerged in the bath, since there was a tendency for condensation on the cooler parts during measurements above room temperature. In this case also, our freezing-point technique proved unsuitable, but a rough indication was obtained by cooling and observing the temperature at which a cloudiness first appeared.

When freezing-points of greater accuracy were required, as in the determination of the molecular weight of triethyltin chloride in benzene, a large cryoscope was used, together with a 10-junction thermocouple, Cambridge Vernier potentiometer, and photoelectric amplifier.[8]

The conductance cell (of cell constant $0{\cdot}28_3$ cm.$^{-1}$) had dip-type electrodes and was immersed in water at 25°. Readings were made on a Mullard conductance bridge.

Attempts to use spectrophotometric cells with optically flat silica faces were unsuccessful, owing to cracking on immersion in liquid nitrogen during the preparation of the mixtures. Finally a simple (cylindrical) silica tube of external diameter 12 mm. (i.d. 10 mm.) was used, and to its upper end were attached, through a graded seal, a glass 4 mm. vacuum tap and a B14 cone. Stirring was accomplished magnetically (iron-in-glass stirrer). The comparison cell contained water and was made from similar silica tubing. These cells were always placed in the spectrophotometer (Unicam SP.500) with the same orientation to minimize the errors inherent in their design. Colours appeared in many of the mixtures investigated, and our results, though limited to the dimethylamine system and not of great precision, suggest that a more extensive spectrophotometric investigation of these systems would be fruitful.

Materials.—Triethyltin chloride, prepared from tetraethyltin and a slight excess of stannic chloride,[9] followed by fractionation twice *in vacuo*, was collected at 68—72°/0·9—1·2 mm. (Found: C, 30·3; H, 6·4; Cl, 15·0. Calc. for $C_6H_{15}ClSn$: C, 29·9; H, 6·3; Cl, 14·7%), m. p. 15·3° (lit.,[10] 15·5°).

The gaseous amines were obtained from commercial cylinders or ampoules and purified by passage through a potassium hydroxide column and fractionation in the vacuum system. Diethylamine and pyridine were fractionated in the vacuum system and stored in ampoules over mercury-shielded stop-cocks. "AnalaR" benzene was twice recrystallized and then distilled over sodium wire.

Results and Discussion

The results are in the Tables and the Figure, which summarizes all the data for the dimethylamine system. (Preliminary, more approximate, freezing-point determinations extending beyond $r = 2$ gave no indication of further solid phases.) Compositions are expressed

[6] Sanderson, "Vacuum Manipulation of Volatile Compounds," Wiley, New York, 1949.
[7] Hammett and Deyrup, *J. Amer. Chem. Soc.*, 1933, **55**, 1900; Gillespie, Hughes, and Ingold, *J.*, 1950, 2473.
[8] Kirkbride and Wyatt, *Trans. Faraday Soc.*, 1958, **54**, 483.
[9] Kozeschkow, *Ber.*, 1933, **66**, 1661.
[10] Grüttner and Krause, *Ber.*, 1917, **50**, 1803.

in terms of r, the ratio of moles of amine to moles of triethyltin chloride. There is clear evidence for the existence of solid compounds containing two triethyltin chloride molecules to one of amine for all the bases studied except pyridine, which seems to form only the 1 : 1 compound as in the Me_3SnCl system.[4] Favourable crystal-packing arrangements are not sufficient to explain these observations, for the spectrophotometric results show that the composition $r = 0{\cdot}5$ corresponds to the maximum absorption by the liquid at the new peak near 300 mμ. (A further, very weak, absorption at 400 mμ became detectable at $r = 1$.) The low vapour pressures of amine at small values of r also strongly indicate chemical reactions, a conclusion which may be strengthened by the observation that in the methylamine–tetraethyltin system, where no compound occurs, there are marked *positive* deviations from Raoult's law [11] (cf. also Greenwood and Wade [12]). Amongst the aliphatic amines, the 2 : 1 and 1 : 1 compounds are more stable for dimethylamine than for diethylamine and trimethylamine, and with the last there is no indication of a 1 : 1 compound in the freezing-point diagram. The extents of the reactions in the liquid cannot be very different for Et_2NH and Me_3N, however, since the vapour pressures of the amine in the two systems at given r values are almost in the same ratio as the vapour pressures of the pure bases at 20°, which are 19·2 (Et_2NH) [13] and 141·5 cm. (Me_3N).[14]

TABLE 1. *Vapour pressures (cm. Hg at 20°) and freezing-points in the triethyltin chloride–amine systems.*

(*a*) Dimethylamine			(*b*) Trimethylamine			(*c*) Diethylamine			(*c*) *contd.*		
r	p	F. p.	r	p	F. p.	r	p	F. p.	r	p	F. p.
0·000	0·06	15·3°	0·049	0·90	14·5°	0·062	0·20	13·0°	0·969	9·29	—
0·034	0·03	14·5	0·112	3·27	8·4	0·129	0·57	8·8	1·042	—	−4·4°
0·094	0·06	12·3	0·189	5·31	5·3	0·200	1·03	3·8	1·020	9·88	—
0·180	0·09	7·6	0·258	9·45	−0·4	0·298	1·81	−3·0	1·196	—	−5·4
0·238	0·25	6·4	0·312	10·30	+1·7	0·356	2·49	−1·7	1·164	10·75	—
0·352	0·42	10·1	0·368	16·94	—	0·418	3·10	−0·4	1·307	—	−6·9
0·431	0·61	13·7	0·409	20·05	7·3	0·453	3·44	+0·5	1·273	11·52	—
0·461	0·69	13·9	0·435	22·29	7·9	0·484	3·78	+0·9	1·378	—	−8·5
0·500	0·89	14·8	0·474	25·48	8·2	9·511	4·11	+0·7	1·342	12·12	—
0·534	1·14	14·3	0·500	27·94	8·3	0·533	4·43	−0·2	1·473	12·82	
0·593	1·37	12·8	0·534	30·46	7·8	0·564	4·71	—	1·595	13·32	
0·665	1·94	11·1	0·566	33·56	7·0	0·662	—	−4·6	1·778	—	−11·5
0·801	3·78	8·9	0·611	37·48	—	0·645	5·84	—	1·737	13·83	—
0·869	5·25	13·3	0·662	—	5·6	0·764	—	−4·8	1·920	—	−12·3
0·929	7·18	14·6	0·685	41·78	—	0·744	7·10	—	1·878	14·16	—
0·977	8·24	14·6	0·747	—	4·6	0·840	—	−4·5	1·956	—	−12·7
1·021	9·67	14·7	0·741	47·48	—	0·814	7·91	—	1·913	14·23	—
1·052	11·12	14·3	0·811	—	2·0	0·907	—	−4·5	1·996	—	−12·9
1·083	12·61	13·8	0·815	54·31	—	0·882	8·54	—	1·953	14·28	—
1·178	18·18	11·3	0·922	—	−1·5	0·933	—	−4·0			
1·280	24·38	9·6	0·903	60·82	—	0·907	8·74	—			
1·384	29·84	6·0	1·043	—	−4·9	0·969	—	−4·1			
1·461	34·65	3·8				0·943	8·88	—			
1·498	36·64					0·996	—	−4·1			

A doubled formula for certain tin(IV) halide compounds (Laubengayer and Smith [15]) might simply explain our 2 : 1 compounds, but since it is difficult to see how the addition of a donor molecule could stabilize a dimer of Et_3SnCl considerably, we regard the following proof of the absence of dimerization of triethyltin chloride in benzene as evidence against such a formulation in this case (see Table 3).

In view of the partially ionic character [16] of triethyltin chloride, we may suppose that it is slightly self-dissociated in the liquid state, yielding the Et_3Sn^+ ion. If the anion can

[11] Joshi, unpublished work.
[12] Greenwood and Wade, *J.*, 1956, 1527; 1957, 1516.
[13] Pohland and Mehl, *Z. phys. Chem.*, 1933, *A*, **164**, 48.
[14] Swift and Hochanadel, *J. Amer. Chem. Soc.*, 1945, **67**, 880.
[15] Laubengayer and Smith, *J. Amer. Chem. Soc.*, 1954, **76**, 5985.
[16] Anderson, *J. Amer. Chem. Soc.*, 1957, **79**, 4913.

be solvated, as $Et_3SnCl_2^-$, the existence of 2 : 1 compounds can be explained by attachment of the amine base (B) to the acceptor Et_3Sn^+:

$$2Et_3SnCl + B \rightleftharpoons Et_3SnB^+ + Et_3SnCl_2^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

Comparison of the conductance with that of other systems (H_2SO_4,[17] $GaCl_3$–$POCl_3$ [12]) indicates that the concentration of free ions may not exceed a few units per cent., so that

TABLE 2. *Freezing-points in the triethyltin chloride–pyridine system.*

r	0·029	0·058	0·101	0·116	0·159	0·25
F. p.	14·8°	12·9°	11·1°	9·6°	21·7°	36°
r	0·37	0·53	0·73	1·00	1·37	1·78
F. p.	49° *	56°	59°	61°	59°	53°

* Results above 50° were not reproducible to better than 1°.

TABLE 3. *Molecular weight of triethyltin chloride in benzene.*

Weight of benzene in cryoscope 54·60 g. (f. p. 5·445°).

Weight of Et_3SnCl added (g.)	0·9673	2·0750	
Depression of f. p. of benzene	0·377°	0·784°	
Molecular wt. of Et_3SnCl	241	249	(Calc. for monomer, 241·3)

At the end of this experiment additions of diethylamine were made and the further depressions of freezing-point showed clearly that the Et_2NH and Et_3SnCl molecules were combining to give fewer particles than would be expected in the absence of any reaction, again confirming that some form of reaction occurs in the liquid.

extensive ion-pairing would also have to be supposed and would indeed be expected. It may therefore be significant that at higher r values ($r > 0·8$) the partial pressures of diethylamine and trimethylamine approximate to the fraction $(2r - 1)/2r$ of the pure amine vapour pressure, which is what would be expected for an ideal solution of ion-pairs of the type, Et_3SnB^+,$Et_3SnCl_2^-$.

Several different explanations, all consistent with eqn. (1), are now possible for the 1 : 1 compounds. Kraus and Greer [4] formulated their Me_3SnCl,C_5H_5N compound as a substituted ammonium halide, which is consistent with (1) if it is supposed that the $Et_3SnCl_2^-$ ion dissociates to give Cl^- as the concentration of triethyltin chloride decreases. Such an explanation throws the responsibility for the change from the 2 : 1 to the 1 : 1 ratio on the anion, however, and does not therefore explain the different behaviour of the bases. A more attractive hypothesis is that the relative acid strengths of Et_3SnB^+ and BH^+ are such that reaction (1) is followed by a proton transfer which gives the 1 : 1 ratio at higher r value, *e.g.*,

$$2Et_3SnCl + 2Me_2NH \rightleftharpoons Et_3SnNMe_2 + Me_2NH_2^+ + Et_3SnCl_2^- \quad . \quad . \quad . \quad . \quad (2)$$

Such a reaction would be more important at low r values for stannic chloride systems (since $Cl_3SnNMe_2H^+$ would be expected to be a stronger acid than $Et_3SnNMe_2H^+$) and could therefore explain the absence of 2 : 1 compounds in those systems. A further advantage of reaction (2) is that Me_3N, which does not form the 1 : 1 " compound," cannot undergo this reaction. But there is then the disadvantage that the same should apply to pyridine.

A simpler explanation of the 1 : 1 compounds is that they are not entirely ionic. Kraus and Greer [4] regarded the undissociated form of their pyridine compound as containing quinquevalent nitrogen. Although such a structure could be reformulated in modern terms as an ion-pair, there is still the possibility that truly non-ionic forms may be present, but with five groups round the tin atom. Bases might then be expected to fall into two

[17] Gillespie and Wasif, *J.*, 1953, 204.

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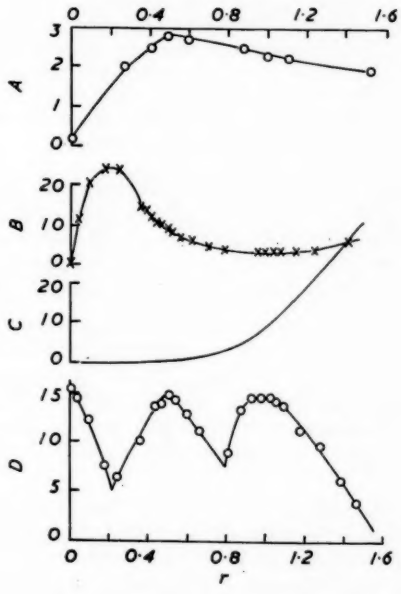
classes in their behaviour towards triethyltin chloride, roughly according to their sizes. Those which are small enough (NH_3,$MeNH_2$) may form 1 : 1 and 1 : 2 co-ordination compounds (with perhaps subsequent reactions [2]) so strongly that any tendency to react according to eqn. (1) is completely masked, whilst larger bases (Et_2NH,Me_3N) react as in (1) because they cannot easily form a fifth group around the tin atom. Pyridine behaves as a relatively small amine [18] and a 1 : 1 compound may also be stabilized in this case by $d\pi$–$p\pi$ bonding (cf. Chatt and Williams [19]).



Properties of the triethyltin chloride–dimethylamine system.
A, Optical density at 300 mμ.
B, Specific conductivity, κ (mmho cm.$^{-1}$).
C, Vapour pressure (cm. Hg.).
D, Freezing point (° c).

Much of the above tentative explanation requires the existence of $Et_3SnCl_2^-$ ions, for which we have no evidence other than the fact that they satisfy the 2 : 1 stoicheiometry [eqn. (1)] and relieve us of the necessity for assuming the presence of $(Et_3SnCl)_2B$ molecules in the solution.

THE UNIVERSITY, SHEFFIELD, 10. [*Received, June 2nd*, 1959.]

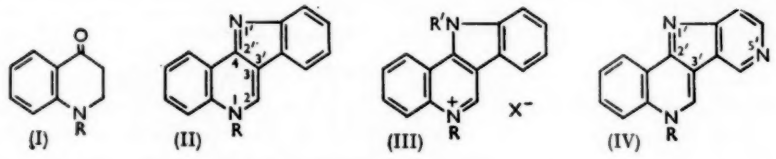
[18] Bjerrum, *Chem. Rev.*, 1950, **46**, 381 (see p. 389).
[19] Chatt and Williams, *J.*, 1954, 4403.

773. *The Structure and Properties of Certain Polycyclic Indolo- and Quinolino-derivatives. Part XIII.* The Cyclisation of Certain 4-Pyridyl- and 4-Quinolyl-hydrazones.*

By Frederick G. Mann, A. F. Prior, and Trevor J. Willcox.

The final stage in the preparation of 4-pyridyl- and 4-quinolyl-hydrazine has been considerably improved. In preliminary work, the 4-pyridyl- and the 4-quinolyl-hydrazone of cyclohexanone have been cyclised to 6,7,8,9-tetrahydro-γ-carboline and its 3,4-benzo-derivative respectively. The main object of the investigation was the similar cyclisation of the corresponding hydrazones of 1,2,3,4-tetrahydro-1-methyl(and -1-phenyl)-4-oxoquinoline, which would have given derivatives of great structural interest, but this cyclisation could not be achieved.

The phenylhydrazone of 1,2,3,4-tetrahydro-4-oxo-1-phenylquinoline [1] (I; R = Ph) and of the 1-methyl analogue [2] (I; R = Me) readily undergo indolisation in boiling ethanolic hydrogen chloride to give the bright yellow 1-phenyl- (and 1-methyl)-ψ-indolo(3′,2′:3,4)-quinoline (II; R = Ph or Me). The latter combine vigorously with acids and with cold alkyl iodides to form salts of structure (III), where R′ represents the proton or the alkyl



(I) (II) (III) (IV)

group, the stability of the system being enhanced by the consequent aromatisation of the pyrrole and the pyridine ring. Many compounds analogous to the oxo-quinolines (I) give similar derivatives.[3]

We have, therefore, investigated the cyclisation of the 4-pyridylhydrazones of the 4-oxo-quinolines (I; R = Ph and Me), to determine whether this process would give compounds of structure (IV) analogous to the ψ-indoloquinolines (II; R = Ph or Me). Compounds such as (IV) would have great interest, because they could react with, for example, one equivalent of methyl iodide in two different ways, each of which would give considerably enhanced stability. Methyl iodide could react to give a compound analogous in structure to (III): alternatively the pyridine-$N_{(5')}$ of the compound (IV) might undergo quaternisation to give a cyanine iodide, which would be markedly stabilised by the canonical forms in which the positive charge was carried by the pyrrole-$N_{(1')}$ or the pyridine-$N_{(1)}$.

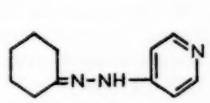
Indolisation of 4-pyridylhydrazones has apparently not been recorded, although the 2-pyridyl-[4] and the 2-methyl-3-pyridyl-hydrazone [5] of cyclohexanone undergo this reaction under more vigorous conditions than the corresponding phenylhydrazones require. A preliminary investigation of the cyclisation of cyclohexanone 4-pyridylhydrazone (V) was therefore undertaken. This hydrazone, when heated with zinc chloride at 240° for 10 min. and then extracted with hydrochloric acid, gave the chlorozincate of 6,7,8,9-tetrahydro-γ-carboline, which with aqueous sodium hydroxide furnished the crystalline base (VI). This compound is isomeric with the 1,2,3,4-tetrahydro-γ-carboline which

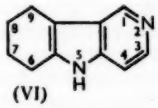
* Part XII, I.G. Hinton and Mann, *J.*, 1959, 2043.

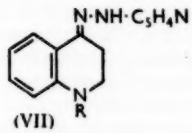
[1] Mann, *J.*, 1949, 2816.
[2] Braunholtz and Mann, *J.*, 1955, 381.
[3] Mann and Smith, *J.*, 1951, 1898; Almond and Mann, *J.*, 1952, 1870.
[4] Okuda and Robison, *J. Amer. Chem. Soc.*, 1959, **81**, 740.
[5] Clemo and Holt, *J.*, 1953, 1313.

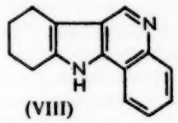
Robinson and Thornley [6] obtained by the reduction of γ-carboline with sodium and butan-1-ol.

Attempts similarly to cyclise tetrahydro-1-methyl-4-oxoquinoline 4-pyridylhydrazone (VII; R = Me) failed however. The hydrazone, when heated with ethanolic hydrogen chloride, or anhydrous zinc chloride, or boron trifluoride in acetic acid,[7] gave the hydrochloride, chlorozincate, and boron trifluoride complex of the unchanged hydrazone.


(V)


(VI)


(VII)


(VIII)

Passage of hydrogen chloride over the molten hydrazone,[8] or treatment with hot acetic–sulphuric acid [9] or polyphosphoric acid,[10] left the hydrazone unaffected or considerably decomposed, and sulphuric acid gave the (?6-)sulphonic acid. Cyclisation of the hydrazone (VII; R = Ph) also failed: this hydrazone was much more readily hydrolysed by acids.

It is noteworthy that similar attempts to indolise cyclohexane-1,2-dione bis-4-pyridylhydrazone either left the hydrazone unaffected or caused decomposition: the hydrazone sublimed when heated at low pressures but at atmospheric pressure decomposed with the formation of 4-aminopyridine. These results contrast strongly with the ready indolisation of cyclohexane-1,2-dione bisphenylhydrazone.[11]

The corresponding derivatives of 4-quinolylhydrazine were therefore investigated. Cyclohexanone 4-quinolylhydrazone with zinc chloride at 245° underwent cyclisation, and the product after considerable purification afforded 6,7,8,9-tetrahydro-3,4-benzo-γ-carboline (VIII).

1,2,3,4-Tetrahydro-1-methyl-4-oxoquinoline 4-quinolylhydrazone, m. p. 210°, was unaffected by zinc chloride at 200° and underwent considerable decomposition at higher temperatures: when it was rapidly heated with zinc chloride to 215° and then basified, the product afforded a crude orange-yellow sublimate, m. p. 370—380°, in insignificant yield. The hydrazone was hydrolysed by boiling ethanolic hydrogen chloride to the hydrazine.

Attempts to prepare compounds of type (IV) or their quinolino-analogues were therefore abandoned.

It is noteworthy that 4-pyridylhydrazine hydrochloride has previously been prepared by heating an ethanolic solution of 4-chloropyridine and hydrazine hydrate in a sealed tube,[12] and 4-quinolylhydrazine hydrochloride by boiling under reflux an aqueous-ethanolic solution of 4-chloroquinoline and hydrazine hydrate.[13] The former preparation is laborious and gives an impure product, while the latter gives a low yield. We find that both these hydrazine salts can readily be prepared pure and in high yield by boiling under reflux a propanolic solution of the 4-chloro-base and pure hydrazine hydrate.

The infrared spectrum of 4-quinolylhydrazine hydrochloride shows two bands, at 3170 and 3285 cm.$^{-1}$ respectively, which in relative intensities and spacing almost undoubtedly indicate an $-NH_2$ group: a shoulder at 3120 cm.$^{-1}$ in the former band may be due to the =NH group. A strong rather broad band at 2790 cm.$^{-1}$, with a subsidiary maximum at 2810 cm.$^{-1}$, almost certainly indicates a $\equiv NH^+$ group. Hence salt formation has occurred on the quinolyl nitrogen atom.

[6] Robinson and Thornley, *J.*, 1924, **125**, 2174.
[7] Snyder and Smith, *J. Amer. Chem. Soc.*, 1943, **65**, 2452.
[8] Robinson and Robinson, *J.*, 1918, **113**, 639.
[9] Clemo and Felton, *J.*, 1951, 677.
[10] Kissman, Farnsworth, and Witkop, *J. Amer. Chem. Soc.*, 1952, **74**, 3948.
[11] Mann and Willcox, *J.*, 1958, 1525.
[12] Koenigs, Weiss, and Zscharn, *Ber.*, 1926, **59**, 317.
[13] Schofield and Swain, *J.*, 1950, 394.

Experimental

M. p.s were determined from room temperature, except those for which the temperature of immersion is noted as (T.I.).

4-Pyridylhydrazine Hydrochloride.—A solution of 4-chloropyridine (12·6 g.) and pure hydrazine hydrate (4·9 g., 1·1 mols.) in propan-1-ol (40 c.c.) was boiled under reflux for 2 hr., the hydrochloride crystallising meanwhile. The mixture was cooled to 0°, and the hydrochloride, when collected, washed with propan-1-ol, and recrystallised from methanol, had m. p. 242—243°: a second crop, obtained from the methanolic mother-liquors by precipitation with ether, and then once recrystallised from methanol, had the same m. p. (Found: N, 29·0. Calc. for $C_5H_7N_3$,HCl; N, 28·9%). The total yield was 14·0 g., 85%. The hydrazine gave a benzaldehyde derivative, pale-grey needles, m. p. 200° (lit.,[12] pale yellow prisms, m. p. 195°).

Cyclohexanone 4-Pyridylhydrazone (V).—A solution of cyclohexanone (2 g.) in acetic acid (4 c.c.) was added to a solution of the above hydrochloride (3·2 g., 1·1 mols.) and crystalline sodium acetate (5·4 g.) in water (6 c.c.), which was boiled under reflux for 3 hr. and then poured into water (20 c.c.) and aqueous ammonia (*d* 0·880; 6 c.c.). After 1 hr. the colourless precipitated *hydrazone* (V) was collected, washed with water, and recrystallised from aqueous methanol (1 : 1 by vol.); it had m. p. 168—170° (darkening) (2·6 g., 70%) (Found: C, 69·7; H, 7·8. $C_{11}H_{15}N_3$ requires C, 69·9; H, 7·9%).

6,7,8,9-Tetrahydro-γ-carboline (VI).—An intimate mixture of the hydrazone (V) (2 g.) and powdered zinc chloride (6 g.) was heated in an oil-bath at 240° for 10 min., and the cold product was extracted with boiling water (40 c.c.) containing dilute hydrochloric acid (5 c.c.). The extract, on cooling, deposited the crystalline *chlorozincate* (2·8 g.), m. p. 275—276° (from very dilute hydrochloric acid), of the carboline (VI) (Found: C, 47·4; H, 4·6; N, 10·5. $2C_{11}H_{12}N_2,H_2ZnCl_4$ requires C, 47·6; H, 4·7; N, 10·2%).

An aqueous solution of this salt, when treated with an excess of aqueous ammonia, deposited a colourless amorphous precipitate. After 4 hr., this was collected, dissolved in aqueous methanol (3 : 1 by vol.), and set aside at 0° overnight. Colourless crystals, m. p. 223—224°, apparently of a *dihydroxydichlorozincate*, were then collected, washed with methanol, and dried at 70°/0·2 mm. [Found: C, 51·4; H, 4·9. $2C_{11}H_{12}N_2,H_2ZnCl_2(OH)_2$ requires C, 51·3; H, 5·1%].

A hot aqueous solution of the chlorozincate, when treated with a large excess of 10% aqueous sodium hydroxide, deposited the *carboline* (VI), which, after being set aside overnight, collected, and recrystallised from aqueous ethanol (1 : 4 by vol.), had m. p. 269—271°, increased to 270—272° after sublimation at 200°/0·1 mm. (Found: C, 77·1; H, 6·6; N, 16·5. $C_{11}H_{12}N_2$ requires C, 76·9; H, 7·0; N, 16·3%).

Dehydrogenation of the carboline with palladium–charcoal was briefly investigated without success.

1,2,3,4-Tetrahydro-1-methyl-4-oxoquinoline 4-Pyridylhydrazone (VII; R = Me).—A solution of the oxoquinoline (I; R = Me) (1·3 g.) in ethanol (12 c.c.) was added to a solution of 4-pyridylhydrazine hydrochloride (3·5 g., 3 mols.) and sodium acetate (9·7 g.) in 40% aqueous acetic acid (16 c.c.), which was boiled under reflux for 5 hr. and then poured into an excess of aqueous ammonia. The yellow gum which was deposited slowly solidified when repeatedly kneaded with hot water; recrystallised from aqueous methanol (1 : 4 by vol.) it gave the yellow *hydrazone* (VII; R = Me) (2 g., 95%), m. p. 181—182°, which darkened slowly on exposure to light (Found: C, 70·9; H, 6·6; N, 22·3. $C_{15}H_{16}N_4$ requires C, 71·3; H, 6·5; N, 22·2%).

A solution of the hydrazone in an excess of methyl iodide when set aside for 1 hr., or in methanolic methyl iodide when boiled under reflux for 1 hr. and cooled, deposited pale yellow crystals of the *monomethiodide*, m. p. 228—229° (from methanol) (Found: N, 14·4. $C_{16}H_{19}N_4I$ requires N, 14·25%). A solution of the hydrazone and methyl iodide in nitromethane, when similarly boiled, deposited the colourless *dimethiodide*, m. p. 202—203° (decomp.) (T.I. 190°) after crystallisation from methanol containing *ca.* 3% of water (Found: C, 38·3; H, 4·1; N, 10·5. $C_{17}H_{22}N_4I_2$ requires C, 38·2; H, 4·0; N, 10·45%).

Attempted Cyclisation of the Hydrazone (VII; R = Me).—(i) The yellow solution of the hydrazone (1 g.) in saturated ethanolic hydrogen chloride (10 g.) rapidly deposited the colourless crystalline hydrochloride, a sample of which had m. p. 182—184° (T.I. 170°), but being very deliquescent was not analysed. The mixture, when boiled under reflux for 5 hr., cooled, and basified with aqueous ammonia, deposited the hydrazone. The use of 2N-hydrochloric acid with heating for 1½ hr. gave the same result.

(ii) An intimate mixture of the hydrazone (0·4 g.) and zinc chloride (2 g.), when heated at

200° for 10 min., effervesced and formed a red liquid. The cold melt was extracted with a minimum of hot 10% hydrochloric acid, and the extract, on the addition of concentrated hydrochloric acid, deposited pale red tabular crystals of the *chlorozincate* of the hydrazone; after recrystallisation from dilute hydrochloric acid this had m. p. 320—322° (from room temperature), 327—330° (T.I. 312°) (Found: C, 38·3; H, 3·5; N, 12·3. $C_{15}H_{16}N_4,H_2ZnCl_4$ requires C, 39·3; H, 3·5; N, 12·2%. Low carbon values were obtained). Further similar recrystallisation gave cream-coloured needles, m. p. 314° (decomp.) (from room temperature), 318° (decomp.; T.I. 310°) (Found: C, 39·2; H, 3·8; N, 12·5%). The two crystalline products may be dimorphic forms, or may be structurally different, possibly in the position of the protons in the cation. A solution of the hydrazone in dilute hydrochloric acid, when added to concentrated aqueous zinc chloride, deposited the cream-coloured salt, m. p. and mixed m. p. 318° (decomp., T.I. 310°) after recrystallisation.

Fusion of the hydrazone with zinc chloride at 270° for 1 hr. gave the same result.

(iii) A 40% solution of boron trifluoride in acetic acid (15 c.c.) was added to one of the hydrazone (0·9 g.) in acetic acid (15 c.c.), which was then boiled under reflux for 1 hr., poured into water, and basified with aqueous ammonia. The lemon-yellow precipitate, when collected, washed, and recrystallised from 50% aqueous ethanol, afforded boron-containing needles (1·1 g.), m. p. 208—210°, insoluble in all the usual solvents. It was unaffected by boiling ethanolic ammonia or pyridine, but hot 10% aqueous sodium hydroxide liberated the original hydrazone, m. p. and mixed m. p. 181—182° (Found: C, 71·5; H, 6·4; N, 22·2%).

(iv) A solution of the hydrazone (0·2 g.) in concentrated sulphuric acid (5 c.c.) was heated at 130° for 10 min., cooled, poured on ice, and basified with ammonia. Long yellow needles of the monohydrated (?6-)*sulphonic acid*, m. p. 344—346° (decomp.), separated and were dried at 200°/0·2 mm. for 5 hr. (Found: C, 51·6; H, 5·25; N, 16·5. $C_{15}H_{16}O_3N_4S,H_2O$ requires C, 51·7; H, 5·45; N, 16·0%) The acid is insoluble in organic solvents but freely soluble in mineral acids and in warm 10% aqueous sodium hydroxide, being reprecipitated when such solutions are neutralised. Its infrared spectrum indicates that it is a zwitterion. The solution of the hydrazone in sulphuric acid was unaffected at room temperature, and at 180° underwent hydrolysis to water-soluble constituents.

1,2,3,4-*Tetrahydro*-4-*oxo*-1-*phenylquinoline* 4-*Pyridylhydrazone* (VII; R = Ph).—A solution of the oxoquinoline (1·76 g.) in ethanol (40 c.c.) was added to 4-pyridylhydrazine hydrochloride (4·64 g., 4 mols.) and hydrated sodium acetate (13 g., 12 mols.) in warm 40% aqueous acetic acid (30 c.c.), which was boiled under reflux for 6 hr., poured into an excess of dilute aqueous ammonia, and cooled to 0°. The precipitated *hydrazone*, when recrystallised from methanol, formed pale yellow plates (2·4 g., 95%), m. p. 212° (darkening) (Found: C, 76·9; H, 5·95; N, 17·7. $C_{20}H_{18}N_4$ requires C, 76·4; H, 5·8; N, 17·8%). The hydrazone forms a colourless *acetate*, m. p. 252° (decomp., T.I. 242°) (from methanol) (Found: C, 71·1; H, 6·1. $C_{20}H_{18}N_4,C_2H_4O_2$ requires C, 70·7; H, 5·95%), and a *monomethiodide*, yellow needles, m. p. 289° (decomp.; T.I. 275°) (from aqueous methanol) (Found: C, 55·2; H, 4·5; N, 12·4. $C_{21}H_{21}N_4I$ requires C, 55·4; H, 4·6; N, 12·3%): only this methiodide was formed when the hydrazone and methyl iodide was boiled in methanol or nitromethane for 30 min.

A mixture of the hydrazone and zinc chloride was heated at 200° until effervescence ceased, and on working up afforded the *chlorozincate* of the hydrazone, which on recrystallisation from water formed very pale pink crystals, melting indefinitely at 225—240° (decomp.) (Found: C, 45·9; H, 4·2; N, 10·2. $C_{20}H_{18}N_4,H_2ZnCl_4$ requires C, 45·9; H, 3·9; N, 10·6%).

Cyclohexane-1,2-*dione Bis*-4-*pyridylhydrazone*.—A solution of the dione (1·8 g.), 4-pyridylhydrazine hydrochloride (5·2 g., 2·2 mols.), and hydrated sodium acetate (12·0 g., 4 mols.) in ethanol (20 c.c.) was heated on a steam-bath under nitrogen for 90 min., cooled, and basified with aqueous ammonia. The precipitated *hydrazone*, when recrystallised from ethyl methyl ketone, formed yellow needles (3 g., 63%), m. p. 223—225°, which were dried at 120°/0·2 mm. for 6 hr. (Found: C, 62·0; H, 6·3; N, 26·25. $C_{16}H_{18}N_6,H_2O$ requires C, 61·8; H, 6·4; N, 26·9%). The hydrazone in ethanol readily gave a *dipicrate*, which after recrystallisation from ethanol melted slowly 130—160° (T.I. 80°) and 130—180° (T.I. 120°) (Found: C, 44·9; H, 3·3; N, 22·35. $C_{16}H_{18}N_6,2C_6H_3O_7N_3$ requires C, 44·7; H, 3·2; N, 22·3%). The hydrazone readily gave a colourless *dimethiodide*, m. p. 236—237° (decomp.) (Found: N, 14·5. $C_{18}H_{24}N_6I_2$ requires N, 14·5%).

The hydrazone when heated at atmospheric pressure gave a distillate of 4-aminopyridine, m. p. 158—161° (lit.,[14] 159—160°) (Found: C, 63·8; H, 6·6; N, 29·9. Calc. for $C_5H_6N_2$:

[14] Leis and Curran, *J. Amer. Chem. Soc.*, 1945, **67**, 79.

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C, 63·8; H, 6·4; N, 29·8%), which gave a *picrate*; precipitated from ethanolic solution and recrystallised from water, this had m. p. 216—218° (lit.,[15] 215—216°, without analytical identification) (Found: C, 41·1; H, 2·4. $C_5H_6N_2,C_6H_3O_7N_3$ requires C, 40·9; H, 2·8%).

4-Quinolylhydrazine Hydrochloride.—Pure hydrazine hydrate (4·4 g., 1·1 mols.) was added to a solution of 4-chloroquinoline (13 g.) in propan-1-ol (40 c.c.), which was boiled under reflux for 90 min. and cooled. The crystalline hydrochloride was collected, washed with propanol, and dried. Hydrogen chloride was passed through the filtrate to precipitate a second crop of the hydrochloride (total yield, 13·5 g., 87%), m. p. 311° (decomp.) (lit.,[15] 300—301°) (Found: C, 55·5; H, 5·4. Calc. for $C_9H_9N_3$,HCl; C, 55·3; H, 5·1%).

Cyclohexanone 4-Quinolylhydrazone.—Cyclohexanone (0·91 g.), 4-quinolylhydrazine hydrochloride (2·0 g., 1·1 mols.), and hydrated sodium acetate (2·52 g., 3 mols.) were added in turn to a mixture of water (6 c.c.) and acetic acid (4 c.c.), which was heated in nitrogen under reflux on a steam-bath for 1 hr., some needles (presumably the hydrazone acetate) being deposited. The cold mixture was basified with dilute ammonia, giving a yellow emulsion which rapidly gave the crystalline *hydrazone* (2·0 g., 90%), m. p. 144—145° after crystallisation from 50% aqueous ethanol (Found: N, 17·5. $C_{15}H_{17}N_3$ requires N, 17·6%).

The addition of hydrogen chloride to the hydrazone, each in ethanolic solution, precipitated the colourless *hydrochloride*, m. p. 329—330° (from ethanol) (Found: N, 15·4. $C_{15}H_{17}N_3$,HCl requires N, 15·2%).

6,7,8,9-*Tetrahydro*-3,4-*benzo*-γ-*carboline* (VIII).—An intimate mixture of this hydrazone (1·5 g.) and zinc chloride (6 g.) was inserted in an oil-bath at 245°, and vigorously stirred until the temperature of the melt attained 235°, and then removed. The yellow glassy product was dissolved in hot dilute hydrochloric acid (30 c.c.) and basified with dilute ammonia. The crude pale yellow carboline was sublimed at 220°/0·2 mm. For further purification, a solution of the carboline in benzene (*ca.* 1 l.) was passed down an alumina column, and afforded an upper brown band and a lower colourless band which was strongly fluorescent in ultraviolet light. The latter band was extracted with methanol and afforded colourless crystals, which were recrystallised from diethyl carbonate and finally sublimed as before to remove tenaciously held solvent. The *carboline* had m. p. 292—293° (Found: C, 80·9; H, 6·6; N, 12·5. $C_{15}H_{14}N_2$ requires C, 81·0; H, 6·35; N, 12·6%): it gave a *picrate*, yellow needles (from ethanol containing 5% of acetone), m. p. 263—266° (T.I. 257°) (Found: C, 55·9; H, 3·7; N, 15·6. $C_{15}H_{14}N_2,C_6H_3O_7N_3$ requires C, 55·9; H, 3·8; N, 15·5%).

A mixture of the carboline and palladium–charcoal, when heated at 250° for 2 hr., gave a very small amount of a colourless sublimate, which was remixed with the charcoal and heated at 250°/0·01 mm., giving a sublimate, m. p. 323—325°, depressed by *ca.* 20° on admixture with the original carboline. This sublimate was insufficient for identification, but it was probably 3,4-benzo-γ-carboline, for which Clemo and Perkin [16] give m. p. "greater than 320°."

1,2,3,4-*Tetrahydro*-1-*methyl*-4-*oxoquinoline 4-Quinolylhydrazone.*—The oxoquinoline (I; R = Me) (0·8 g.), 4-quinolylhydrazine hydrochloride (2·0 g., 2 mols.), and hydrated sodium acetate (5 g.) were added to 40% aqueous acetic acid (20 c.c.), which was boiled for 4 hr., cooled, and poured into dilute ammonia. The precipitated solid was collected, washed, and dissolved in acetone, from which, on the careful addition of water, the *hydrazone* separated as yellow needles, m. p. 210° (Found: C, 76·0; H, 6·1; N, 18·9. $C_{19}H_{18}N_4$ requires C, 75·7; H, 6·0; N, 18·6%). The hydrazone in ethanolic solution gave an orange *picrate*, m. p. 232—234°, after collection and washing with hot methanol: it was insoluble in the usual solvents (Found: N, 18·7. $C_{19}H_{18}N_4,C_6H_3O_7N_3$ requires N, 18·5%).

This hydrazone when heated with zinc chloride at 200° was recovered unchanged but at higher temperatures decomposed considerably. A mixture of the hydrazone (0·3 g.) and zinc chloride (1·2 g.) was immersed in a bath at 255° and stirred vigorously until the temperature reached 215°: it was then cooled, digested with dilute hydrochloric acid (10 c.c.), and basified with ammonia. The orange-red deposit when heated at *ca.* 200°/0·01 mm. gave an orange-yellow sublimate, m. p. 370—380°, in too minute yield for identification.

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[15] Koenigs, Kinne, and Weiss, *Ber.*, 1924, **57**, 1175.
[16] Clemo and Perkin, *J.*, 1924, **125**, 1618.

774. *Peroxides of Elements other than Carbon. Part VI.*[1] *Peroxides of Germanium.*

By Alwyn G. Davies and C. D. Hall.

A number of peroxides of germanium have been prepared by treating alkylgermanium halides or germanium tetrachloride with alkyl hydroperoxides or hydrogen peroxide in the presence of a base under anhydrous conditions.

No peroxides of germanium appear to have been described. An obvious likely route to these compounds, by analogy with the preparation of the peroxysilanes,[2] would be the nucleophilic substitution by an alkyl hydroperoxide or hydrogen peroxide at a germanium atom, *e.g.*:

$$n\text{RO·OH} + \text{R}'_{4-n}\text{GeCl}_n \longrightarrow \text{R}'_{4-n}\text{Ge(O·OR)}_n + n\text{HCl} \quad (n = 1\text{—}4)$$

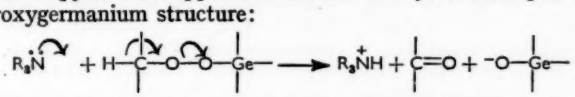
Reactions of this type have now been investigated.

Alkyl hydroperoxides and germanium chlorides react together readily in pentane, cyclohexane, or ether, in the presence of ammonia or triethylamine. The amine hydrochloride can be filtered off under anhydrous conditions, and the product isolated by distillation or crystallisation. By this method a number of organoperoxygermanium compounds have been prepared and characterised; typical examples are tripropyl(t-butylperoxy)germanium, bis(decahydro-9-naphthylperoxy)dipropylgermanium, cyclopentamethylenedi-(t-butylperoxy)germanium, and tetrakis(decahydro-9-naphthylperoxy)germanium. The analogous reaction of anhydrous hydrogen peroxide with tripropylgermanium chloride gave bis(tripropylgermanium)peroxide, $\text{Pr}_3\text{Ge·O·O·GePr}_3$.

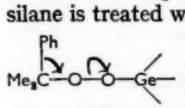
Our preliminary note [3] prompted Rieche and Dahlmann to report their results which have been obtained concurrently and independently.[4] They have prepared germanium peroxides $\text{Ph}_3\text{Ge·O·OR}$ (R = CMe_3, CMe_2Ph, and CPh_3), and bis(triphenylgermanium) peroxide, $\text{Ph}_3\text{Ge·O·O·GePh}_3$, by treating triphenylgermanium bromide successively with ammonia and the appropriate hydroperoxide or hydrogen peroxide, or with the anhydrous sodium salt of the hydroperoxide.

The germanium peroxides which we have prepared are stable up to about 70° for short periods, but some decomposition apparently occurs during distillation above this temperature. They catalyse the polymerisation of vinyl monomers, indicating that O–O homolysis can take place. All the peroxides are readily hydrolysed, and the hydroperoxide can be recovered; for example, tetrakis(decahydro-9-naphthylperoxy)germanium gives germanium dioxide and decahydro-9-naphthyl hydroperoxide.

1,2,3,4-Tetrahydro-1-naphthyl hydroperoxide and germanium tetrachloride in the presence of pyridine gave 1,2,3,4-tetrahydro-1-oxonaphthalene. As the hydroperoxide alone is stable towards pyridine, it appears that a base-catalysed decomposition is occurring in the s-alkylperoxygermanium structure:



A similar decomposition takes place when trimethyl-(1,2,3,4-tetrahydro-1-naphthylperoxy)-silane is treated with triethylamine.[2]

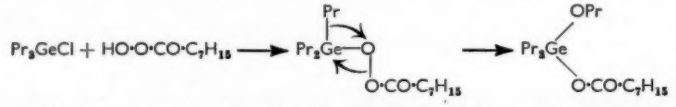


(A)

The product of the reaction between 1-methyl-1-phenylethyl hydroperoxide and germanium tetrachloride became non-peroxidic in the course of a few days, liberating phenol. This reaction probably occurs by a nucleophilic migration of a phenyl group from carbon to oxygen in the structure (A), as is recognised in other derivatives of the hydroperoxide.[5]

[1] Part V, Davies and Packer, *J.*, 1959, 3164.
[2] Part I, Buncel and Davies, *J.*, 1958, 1550.
[3] Davies and Hall, *Chem. and Ind.*, 1958, 1695.
[4] Rieche and Dahlmann, *Angew. Chem.*, 1959, **71**, 169.
[5] Part II, Davies and Moodie, *J.*, 1958, 2372.

Buncel and Davies [2] showed that alkylchlorosilanes with peroxyacids gave non-peroxidic compounds which could be accounted for by assuming the nucleophilic rearrangement of an alkyl group from silicon to oxygen. A similar rearrangement apparently occurs when alkylgermanium chlorides are treated with peroxyacids, *e.g.*:



These peroxides of germanium are therefore on the whole very similar to the analogous peroxides of silicon. An apparent difference, however, arose in attempts to prepare propyltri-(t-butylperoxy)germanium and tetra-(t-butylperoxy)germanium; products with a low peroxide content were isolated, although tetrakis(decahydro-9-naphthylperoxy)germanium and tri- and tetra-(t-butylperoxy)silicon compounds can be isolated. This apparent decomposition may result from partial hydrolysis, despite our precautions, but we believe it may indicate a more fundamental instability. Discussion of this will be deferred until present work on the peroxides of other metals is completed.

Experimental

Analysis.—Peroxidic oxygen was determined iodometrically.

Compounds which gave germanium dioxide on hydrolysis were analysed for germanium gravimetrically, after ignition, as GeO_2, or volumetrically by titration with sodium hydroxide in the presence of glycerol, phenolphthalein being used as indicator. No method could be found which gave consistent results for compounds containing Ge–C bonds.

Microanalyses for carbon often gave low results, probably because some carbide was formed during combustion.

Preparation of Germanium Peroxides.—In these preparations the precautions against explosion described in Part I were observed;[2] in fact, no trouble was encountered. No quantitative investigation of the sensitivity of the germanium peroxides was carried out, but they gave the impression of being less liable to detonate than the silicon peroxides.

Peroxides of germanium

			Found (%)			Reqd. (%)		
Compound	B. p.	Press. (mm.)	C	H	Perox. O	C	H	Perox. O
1 $Ge(O{\cdot}OC_{10}H_{17})_4$ [a]	—	—	62·6	9·5	16·5	64·1	9·1	17·1
2 $Pr_2Ge(O{\cdot}OC_{10}H_{17})_2$	>95° (bath)	0·01	—	—	11·8	—	—	12·9
3 $[CH_2]_5{>}Ge(O{\cdot}OBu^t)_2$ ...	60°	0·001	45·7	8·4	19·1	48·8	8·7	19·9
4 $Me_2Ge{\cdot}O{\cdot}OC_{10}H_{17}$	65° (bath)	0·5	—	—	10·6	—	—	11·1
5 $Pr_3Ge{\cdot}O{\cdot}OBu^t$	35°	0·001	52·5	10·4	10·2	53·7	10·3	11·0
6 $Pr_3Ge{\cdot}O{\cdot}OC_{10}H_{17}$	65—70° (bath)	0·01	60·0	10·2	7·5	61·5	10·2	8·6
7 $Pr_3Ge{\cdot}O{\cdot}O{\cdot}GePr_3$ [b]	60—70° (bath)	0·05	47·2	9·4	6·3	49·7	9·7	7·4

[a] $C_{10}H_{17}$ = decahydro-9-naphthyl. [b] Prepared by using 100% H_2O_2 in ether. M. p.s: (1) 84—85°; (3) −35°; (6) *ca.* 20°. n_D^{26} (3) 1·4553; (5) 1·4383; (6) 1·4779; (7) 1·4608.

The germanium peroxides are readily hydrolysed and were exposed only to the atmosphere of a dry (P_2O_5) glove-box. All solvents and reactants were thoroughly dried; ammonia was obtained from the liquid dried with sodium. Some of the peroxides were distilled in the molecular still illustrated in Part II.[5]

The preparation of one germanium peroxide is described in detail; the others were prepared by similar methods. Ammonia was an alternative catalyst, and frequently the reaction was conducted completely at room temperature.

Tetrakis(decahydro-9-naphthylperoxy)germanium.—Germanium tetrachloride (0·3 g.) in pentane (5 c.c.) was added dropwise at room temperature to a stirred solution of the hydroperoxide (1·0 g.) and triethylamine (0·5 g.) in pentane (20 c.c.) and ether (5 c.c.); the amine hydrochloride was immediately precipitated. The mixture was heated under reflux for 0·5 hr., and the triethylammonium chloride, m. p. 251—253° (decomp.) (0·70 g.; calc., 0·70 g.), was

filtered off in the glove-box. The solvent was removed from the filtrate under reduced pressure, leaving a white crystalline solid (0·8 g.) which was recrystallised from pentane at −70°, giving *tetrakis(decahydro-9-naphthylperoxy)germanium*, m. p. 84—85° [Found: C, 62·6; H, 9·5; Ge (gravimetrically), 9·2, (volumetrically), 10·1; peroxidic O, 16·5. $Ge(O_2C_{10}H_{17})_4$ requires C, 64·1; H, 9·1; Ge, 9·7; peroxidic O, 17·1%].

Infrared Spectra.—The infrared spectra of tripropyl-(t-butylperoxy)germanium, (decahydro-9-naphthylperoxy)tripropylgermanium, bistripropylgermanium peroxide, and cyclopentamethylenedi-(t-butylperoxy)germanium were determined. All gave bands between 11·70 and 11·95 μ and between 9·90 and 10·08 μ, and a series from 7·0 to 8·5 μ; these appear to be characteristic of the Ge–C bond.[6] Bands at 9·70 μ (weak) and 14·50—14·80 μ (strong) were also common to all four compounds; these bands are also present in the spectra of germanium tetra-alkoxides.[7] The characteristic absorption of the peroxide group at about 11·65 μ appeared only as a shoulder on the peak ascribed to the Ge–C bond.

Reaction between 1-Methyl-1-phenylethyl Hydroperoxide and Germanium Tetrachloride.—Treatment of germanium tetrachloride with the hydroperoxide in the presence of triethylamine gave a pale yellow liquid [Found: peroxidic O, 15·8. Calc. for $Ge(O_2C_9H_{11})_4$: peroxidic O, 18·9%]. After 2 days it had a dark red-brown colour and smelled strongly of phenol (Found: peroxidic O, 5%). When an attempt was made to distil the peroxide at 75° (bath)/0·01 mm., rapid decomposition occurred.

Reaction between 1,2,3,4-Tetrahydro-1-naphthyl Hydroperoxide and Germanium Tetrachloride.—A solution of the hydroperoxide and pyridine in pentane–ether was treated with germanium tetrachloride, yielding a white precipitate. The mixture was stirred for 1 hr., and the pyridine hydrochloride filtered off. Analysis of a portion of the filtrate showed that only 20% of the original peroxide remained. The solvent was removed at 15 mm., leaving 1,2,3,4-tetrahydro-1-oxonaphthalene (2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 255—257°).

Reaction between t-Butyl Hydroperoxide and Germanium Tetrachloride.—A solution of germanium tetrachloride (0·5 g.) in pentane (5 c.c.) was added dropwise at room temperature to a stirred solution of t-butyl hydroperoxide (0·95 g.) and triethylamine (0·94 g.) in pentane (20 c.c.). After 20 min., triethylammonium chloride, m. p. 249—251° (decomp.) (1·3 g.; calc., 1·3 g.), was filtered off. Analysis of a portion of the filtrate showed that 76% of the original peroxide remained. Removal of the solvent at 40° (bath)/15 mm. left a colourless liquid (0·5 g.) [Found: Ge, 15·4; peroxidic O, 22·2. Calc. for $Ge(O_2C_4H_9)_4$: Ge, 16·9; peroxidic O, 29·8; for $Ge(OC_4H_9)(O_2C_4H_9)_3$: Ge, 17·3; peroxidic O, 23·3%]. Similarly, on use of ammonia as the catalyst, ammonium chloride was precipitated quantitatively. A viscous liquid was recovered which could not be distilled in the molecular still (Found: peroxidic O, 21·1%); in air it rapidly gave a white solid.

Reaction between t-Butyl Hydroperoxide and Propylgermanium Trichloride.—n-Propylgermanium trichloride (2·0 g.) in pentane (5 c.c.) was added dropwise at 20° to a solution of the hydroperoxide (2·8 g.) and triethylamine (2·8 g.) in pentane (35 c.c.). The mixture was heated under reflux for 0·5 hr., and filtered free from the amine hydrochloride (3·4 g., calc., 3·7 g.), and the pentane removed at 14 mm., leaving a colourless liquid (2·9 g.; calc., 3·9 g.) [Found: peroxidic O, 21·9. Calc. for $PrGe(O_2Bu)_3$: peroxidic O, 25·1%]. Distillation in the molecular still gave what was apparently *-n-propyldi-(t-butylperoxy)germanium oxide*, b. p. 60° (bath)/0·001 mm. [Found: C, 44·6; H, 8·6; peroxidic O, 21·0. $[(BuO_2)_2PrGe]_2O$ requires C, 43·8; H, 8·3; peroxidic O, 21·1%]. The infrared spectrum showed no evidence of an OH group,[7] rendering it unlikely that the product was the hydroxide corresponding to the above compound, which has a somewhat similar analysis.

Reaction between Tripropylgermanium Chloride and Peroxyoctanoic Acid.—Triethylamine (0·43 g.) was added at 20° to a stirred solution of tripropylgermanium chloride (1·0 g.) and peroxyoctanoic acid (0·7 g.) in pentane (25 c.c.). The amine hydrochloride was immediately precipitated and was filtered off after 15 min. (0·45 g.; calc., 0·55 g.). The solvent was removed from the filtrate at 15 mm., leaving a liquid (1·2 g.) (Found: peroxidic O, 0·3%), b. p. 100° (bath)/0·02 mm. (0·9 g.), n_D^{25} 1·4514 [Found: C, 57·7; H, 10·5%; *M* (by titration with NaOH), 364. Calc. for $Pr_2Ge(OPr)(O_2C_8H_{15})$: C, 56·6; H, 10·0%; *M*, 361]. Part was neutralised

[6] Rochow, Hurd, and Lewis, "The Chemistry of Organometallic Compounds," Wiley, New York, 1957, p. 169; Rochow, Didtschenko, and West, *J. Amer. Chem. Soc.*, 1951, **73**, 5486; West, *ibid.*, 1953, **75**, 6080.

[7] Johnson and Fritz, *ibid.*, 1953, **75**, 718.

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with aqueous sodium hydroxide, giving octanoic acid which was isolated as its S-*benzylisothiuronium salt*, m. p. and mixed m. p. 154° (Found: C, 61·8; H, 8·7; S, 10·2. $C_{16}H_{18}O_2N_2S$ requires C, 61·9; H, 8·4; S, 10·3%). The remainder of the liquid was hydrolysed with dilute sulphuric acid; an ethereal extract showed the presence of a trace of propyl alcohol on the vapour-phase chromatogram.

We are indebted to Professors E. D. Hughes, F.R.S., and Sir Christopher Ingold, F.R.S., for their interest and encouragement, and to Imperial Chemical Industries Limited (Dyestuffs Division) for grants (to C.D.H.).

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775. *Electrophoresis of Gold and Silver Particles.*

By J. T. HARRISON and G. A. H. ELTON.

The electrophoretic behaviour of particles of gold and silver in suspension in aqueous electrolytic solutions has been studied. Although the particles are conducting, the electrokinetic potentials calculated from the electrophoretic velocities, with the assumption that they are non-conducting, give results in reasonable agreement with those obtained from measurements of streaming currents. An explanation for this observation is suggested. The data are used to calculate electrokinetic charge densities for the various systems studied, and the adsorption of various ions by gold and silver is discussed.

THE electrokinetic potential (ζ) at the metal–solution interface is important in connection with adsorption and corrosion processes. In the past its determination has proved difficult because of the conducting nature of the metal which has rendered the usual techniques for measuring ζ inapplicable. For example, Kruyt and Oosterman [1] and Zackryawski [2] have pointed out the difficulties encountered in attempting to measure ζ-potentials with metallic capillaries by use of the streaming potential technique.

Eversole and Boardman [3] measured the streaming current through a platinum capillary by using an external measuring circuit with a resistance much lower than that of the capillary wall itself. Recently Hurd and Hackerman [4] have improved this technique, and used it to determine the ζ-potentials of gold, platinum, and silver in distilled water, and in dilute solutions of potassium chloride and potassium hydroxide.

The more conventional method of measuring ζ-potentials, namely, that of electrophoresis, has been somewhat neglected in this particular field, because it has been considered that the theory and assumptions involving the boundary conditions embodied in the classical theories of electrophoresis [5,6] would be no longer valid for conducting particles, where some kind of charge transfer involving discharge of ions takes place at the solid–liquid interface.

However, it appears that metals often behave effectively as non-conductors in electrophoresis, since the mobilities of colloidal metal particles are usually of the same order of magnitude as those of non-conducting particles. If Henry's theory [6] applied strictly, the mobilities would be extremely small, as the conductivity of the metal would be large compared with that of the electrolyte. The absence of conduction may be due either to

[1] Kruyt and Oosterman, *Kolloid-Beih.*, 1938, **48**, 377.
[2] Zackryawski, *Phys. Z.*, 1900, **2**, 146.
[3] Eversole and Boardman, *J. Phys. Chem.*, 1942, **46**, 914.
[4] Hurd and Hackerman, *J. Electrochem. Soc.*, (*a*) 1955, **102**, 571; (*b*) 1956, **103**, 316.
[5] Smoluchowski, *Bull. Acad. Sci. Cracovie*, 1903, 182; Huckel, *Phys. Z.*, 1924, **25**, 205.
[6] Henry, *Proc. Roy. Soc.*, 1931, *A*, **133**, 106.

the presence of a thin layer of non-conducting material (*e.g.*, oxide or hydroxide) between the metal and the electrolyte, or to polarisation at the metal–solution interface.[7,8]

The present paper, part of a study of adsorptive properties of noble-metal powders, deals with the application of the electrophoretic technique to suspensions of metal particles in aqueous media.

Experimental

Materials.—Silver and gold were chosen in order to avoid corrosion difficulties.

Silver powder was prepared by electrochemical precipitation from silver nitrate solution by fine copper powder previously cleaned in warm 5% oxalic acid solution. The precipitated silver was washed in alcohol, and a sample of silver powder, particle size ~6 μ, was separated by fractional sedimentation. This sample was thoroughly washed in conductivity water before being treated with dilute ammonia solution to remove silver oxide. It was finally washed six times with conductivity water by successive centrifugation and resuspension.

Gold powder, particle size ~2 μ, was separated from a spectrographically pure sample supplied by Johnson, Matthey and Co. The sample was washed in dilute ammonia solution, degreased in acetone and ether, and finally washed for several days in successive changes of conductivity water.

" Stock " solutions, containing approximately 1% of the metal powder, were made up in conductivity water, and aged for two days before being diluted 100-fold for use. Although none of the dilute suspensions showed any ageing effects, one hour was allowed to elapse before electrophoretic examination.

Electrolytes used in the examination were potassium chloride, barium chloride, lanthanum chloride, hydrochloric acid, and sodium hydroxide. Wherever possible, these were prepared from " AnalaR " materials by further recrystallisation. The last three substances were standardised by conventional techniques. Solutions were prepared from conductivity water, obtained by passing good-quality distilled water through a mixed-bed ion-exchange column. The specific conductivity of the water was in the neighbourhood of 1×10^{-6} ohm^{-1} cm.$^{-1}$.

Apparatus.—Electrophoretic velocities were determined by a micro-electrophoretic technique, using an apparatus similar to that described by Alexander and Saggers.[9] The optical system was arranged to allow horizontal viewing of the particles, in order that the suspension might be in focus for as long as possible.

A Mattson [10] type electrophoresis cell (with grey platinum electrodes), immersed in a water bath at room temperature, was used. The " zero level " was located by application of Henry's optical formula.[11] The mobility of approximately 40 particles was recorded in both directions for each suspension. Although the scatter was sometimes quite large (±10%), the average value was reproducible within 5%. When the mobility was rather small (<10^{-4} cm.^{2} volt^{-1} sec.$^{-1}$), a velocity–depth graph was constructed, and the velocity at the zero level determined by interpolation.

Measurements of electrophoretic velocities in the various electrolyte solutions were made over the range of concentration 10^{-5}N—10^{-2}N.

All experiments were carried out at room temperature (20° ± 5°), and the appropriate values of physical constants, such as viscosity and dielectric constant, were used in each case. No significant trend in ζ-potential with temperature was observed.

Results

ζ-Potentials were calculated from the well-known electrophoresis equation:

$$\zeta = \frac{f\pi\eta V_e}{DE} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where V_e is the electrophoretic velocity in cm./sec. under an applied field strength E (e.s.u./cm.) and D and η are the dielectric constant and viscosity of the dispersion medium respectively: f is a numerical factor whose value depends upon the size and shape of the dispersed particles and the thickness of the ionic double layer surrounding them ($1/\kappa$).

[7] Frumkin, *J. Colloid Sci.*, 1946, **11**, 277.
[8] Kruyt, " Colloid Science," Elsevier, London, 1952, Vol. I, pp. 209, 236.
[9] Alexander and Saggers, *J. Sci. Instr.*, 1948, **25**, 374.
[10] Mattson, *J. Phys. Chem.*, 1933, **37**, 223.
[11] Henry, *J.*, 1938, 997.

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The value of f can be computed from Henry's equation [12] and when $\kappa a > 100$ (where a is the radius of the particle), $f \longrightarrow 4$, and is independent of the particle shape.

In the present work, this condition was only satisfied in the more concentrated solutions, *viz.*, $>ca.\ 5 \times 10^{-4}$N for gold suspensions and $>ca.\ 10^{-4}$N for silver suspensions. However, the correction to be applied was rather small, *e.g.*, in 5×10^{-5}N solutions the correction was 11% for gold suspensions and 4% for silver suspensions.

The variation of ζ-potential (calculated in this way) with concentration is illustrated in Figs. 1 and 2.

An attempt was also made to compute the effect of the " time of relaxation " and surface conductance upon the ζ-potential. The effect of the former will be small in uni-univalent electrolytes,[8] and can be neglected. The results of the analysis using Overbeek's equation [12] for barium chloride and lanthanum chloride suspensions are recorded in Table 1 where ζ′ and f' refer to the corrected values of the electrokinetic potential and the " Henry factor " respectively.

TABLE 1. *Corrections for relaxation effect in* $BaCl_2$ *and* $LaCl_3$ *suspensions.*

System	Normality	ζ (mv)	$1/f$	ζ′ (mv)	$1/f'$
Au–$BaCl_2$	10^{-5}	41·1	4·57	46·3	4·95
,,	5×10^{-5}	33·1	4·23	34·2	4·37
,,	10^{-4}	29·8	4·17	30·2	4·23
Ag–$BaCl_2$	10^{-5}	28·9	4·21	29·7	4·32
,,	5×10^{-5}	24·0	4·10	24·0	4·10
Au–$LaCl_3$	10^{-5}	22·5	4·35	23·7	4·58
,,	5×10^{-5}	13·7	4·16	13·8	4·17
,,	10^{-4}	9·7	4·13	9·7	4·13
Ag–$LaCl_3$	10^{-5}	11·4	4·21	11·4	4·21

The corrections to be applied are negligible at all concentrations for silver suspensions; for gold, the corrections are negligible when the ionic concentration is greater than 5×10^{-5}N.

Booth [13] and Henry [14] have shown theoretically that the effect of surface conductance would be to lower the mobility of a particle by a factor $1 + (\lambda_s/\lambda a)$ where λ_s is the surface conductance and λ is the bulk conductance.

The theoretical surface conductance can be calculated from Urban, White, and Strassner's equation, derived [15] on the basis of a simple double-layer theory. This was done for the metal–KCl and metal–HCl interfaces, and the results are recorded in Table 2, together with the

TABLE 2. *Electrokinetic potentials corrected for surface conductance.*

System	Normality	ζ (mv)	$10^{10}\lambda_s$ (ohm^{-1})	λ (ohm^{-1} cm.$^{-1}$)	$\lambda_s/\lambda a$	ζ′ (mv)
Au–HCl	1×10^{-5}	25·6	0·41	$4{\cdot}259 \times 10^{-6}$	0·096	28·1
,,	5×10^{-5}	18·0	0·57	$2{\cdot}125 \times 10^{-5}$	0·026	18·5
,,	1×10^{-4}	14·9	0·63	$4{\cdot}243 \times 10^{-5}$	0·015	15·1
Ag–HCl	1×10^{-5}	37·5	0·67	$4{\cdot}259 \times 10^{-6}$	0·052	39·5
,,	5×10^{-5}	26·7	0·97	$2{\cdot}125 \times 10^{-5}$	0·015	27·1
,,	1×10^{-4}	18·6	0·85	$4{\cdot}243 \times 10^{-5}$	0·007	18·8
Au–KCl	1×10^{-5}	45·0	0·17	$1{\cdot}490 \times 10^{-6}$	0·113	50·1
,,	5×10^{-5}	41·0	0·30	$7{\cdot}420 \times 10^{-6}$	0·040	42·7
,,	1×10^{-4}	37·7	0·36	$1{\cdot}480 \times 10^{-5}$	0·024	38·6
Ag–KCl	1×10^{-5}	44·0	0·17	$1{\cdot}490 \times 10^{-6}$	0·036	45·6
,,	5×10^{-5}	40·5	0·30	$7{\cdot}420 \times 10^{-6}$	0·013	41·0
,,	1×10^{-4}	38·9	0·40	$1{\cdot}480 \times 10^{-5}$	0·009	39·3

corrected ζ′ values. However, the experimental data tabulated in the literature [8] suggest that theoretical values for surface conductivity are somewhat lower than experimental values. For this reason, the corrected ζ-potential in Table 2 may be somewhat lower than the " true " value.

As it is, the application of the correction leads to a 10% increase in the value of ζ calculated for suspensions of gold in 10^{-5}N solutions, and about 2% in 10^{-4}N solutions; with silver the corresponding corrections are about 4%, and less than 1%, respectively.

[12] Overbeek, " Advances in Colloid Science," Interscience, New York, 1950, Vol. III, p. 113.
[13] Booth, *Trans. Faraday Soc.*, 1948, **44**, 955.
[14] Henry, *ibid.*, p. 1021.
[15] Urban, White, and Strassner, *J. Phys. Chem.*, 1935, **39**, 311.

In calculating the charge per unit area of surface (σ_s) from the ζ-potential, the expression given by Verwey and Overbeek [16] for an infinitely large plane interface, was used:

$$\sigma_s = \left(\frac{NDkTC}{2\pi}\right)^{\frac{1}{2}}\left\{\frac{1}{z_-}\left[\exp\left(z_-e\zeta/kT\right) - 1\right] + \frac{1}{z_+}\left[\exp\left(-z_+e\zeta/kT\right) - 1\right]\right\}^{\frac{1}{2}}$$

where T is the absolute temperature, C the ionic concentration, and z_+ and z_- are the valencies of the cation and anion respectively.

The assumptions implicit in the use of this equation are (*a*) that it can be used for double layers of finite size,[17] and (*b*) that the boundary between the Stern and Gouy layers coincides with the electrokinetic slipping plane, hence ψ_d the boundary potential, can be equated to ζ.

Discussion

(a) *Comparison of the Results with Those obtained from Streaming Currents.*—The only reliable electrokinetic data available for the gold– and silver–solution interfaces are those of Hurd and Hackerman,[4b] which are given in Table 3 for comparison.

Table 3. *Graphical electrokinetic potential data of Hurd and Hackerman by the streaming current technique.*

	ζ-Potential (mv)				ζ-Potential (mv)		
Normality	Au–KCl	Au–KOH	Ag–KCl	Normality	Au–KCl	Au–KOH	Ag–KCl
1×10^{-5}	54	65	55	5×10^{-4}	32	78	23
5×10^{-5}	48	73	43	1×10^{-3}	24	67	18
1×10^{-4}	44	80	36				

For the gold–potassium chloride system, the micro-electrophoretic technique gives results which are *ca.* 5 mv more positive than those of Hurd and Hackerman. However, this difference decreases with increasing electrolyte concentration, and at 10^{-3}N identical ζ-potentials (24 mv) are obtained. For the silver–potassium chloride interface there is good agreement over the middle portion of the concentration range studied, but in dilute solution (10^{-5}N) and in concentrated solution (10^{-3}N) the ζ values differ by *ca.* 10 mv. (Hurd and Hackerman reported variations of ± 4 mv in the results obtained with different silver capillaries in distilled water, although they did not record the degree of variation in potassium chloride.)

It was also possible to compare our results for the gold–sodium hydroxide interface with those of Hurd and Hackerman for the gold–potassium hydroxide interface, since the two cations, sodium and potassium, have similar adsorption properties. Although the variation of ζ with concentration is similar in the two cases, the values differ by *ca.* 20 mv.

It is realised that this type of comparison is restricted, even when the adsorbents are identical, because ultimately their surface properties depend upon their pretreatment. Any difference in the character of the surfaces studied would probably be more apparent in alkaline solutions than in neutral salt solutions, owing to specific adsorption of the hydroxide ion.

In fact, Hurd and Hackerman etched their metal capillaries with dilute acid and followed this with copious washing, a treatment which would tend to activate the surface and probably result in greater adsorption of hydroxide ion.

The great difficulty usually experienced in reproducing electrokinetic results of other workers, even using the same technique, being borne in mind, there is satisfactory agreement between our results (from electrophoretic data and the assumption that the particles are effectively non-conducting) and those of Hurd and Hackerman (from streaming current).

[16] Verwey and Overbeek, "Theory of the Stability of Lyophobic Colloids," Elsevier, London, 1948, p. 33.
[17] Müller, *Kolloid-Beih.*, 1928, **26**, 257.

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Overbeek [12] states that complete electrical polarisation of small metallic particles can be produced by a polarisation tension of a few microvolts. In the present experiments, where particles with diameters of the order of 10 μ were subject to an electrical field of strength about 10 volts/cm. the polarisation potential over the particle was of the order

FIG. 1. *Gold suspensions.*

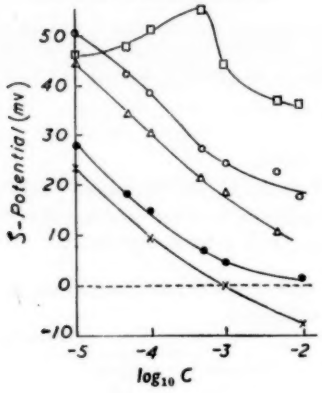


FIG. 2. *Silver suspensions.*

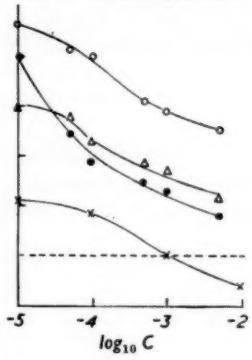


FIG. 3. *Gold suspensions.*

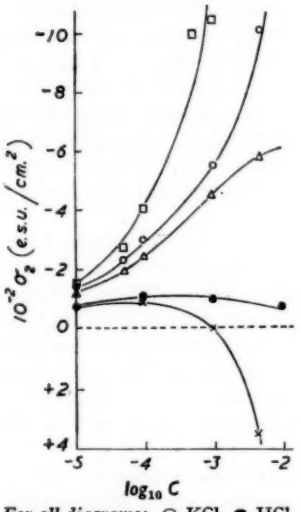
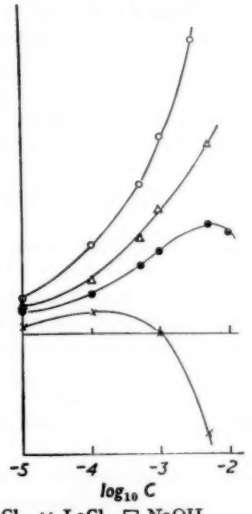


FIG. 4. *Silver suspensions.*



For all diagrams: ○ KCl, ● HCl, △ $BaCl_2$, × $LaCl_3$, □ NaOH.

of 10 mv, so that virtually complete polarisation would occur. In these circumstances, use of the electrophoretic method for metallic particles appears to be permissible.

(b) *Adsorption of Ions by Gold and Silver.*—The ζ-potential at the metal–solution interface, for all the electrolytes studied here, was negative in dilute solutions, indicating a preponderance of anions in the fixed part of the electrical double layer. As the ionic content of the suspension was increased the ζ-potential decreased, the rate of decrease depending upon the type of cation present (Figs. 1 and 2). The increasing negative charge

indicates that preferential adsorption of the anion is taking place, except in the case of lanthanum chloride suspensions at ionic concentrations greater than 10^{-3}N, where ζ (and hence σ_2) becomes positive.

For both barium chloride and lanthanum chloride solutions, the charges and potentials are lower than for corresponding concentrations of potassium chloride, owing to the increased ease with which the bi-valent and ter-valent cations are taken into the fixed (Stern) part of the double layer. By comparing the values of σ_2 for the highest electrolyte concentrations studied (Figs. 3 and 4), the following cation adsorption series can be derived: $K^+ < Ba^{2+} < H^+ < La^{3+}$. On general grounds, it is to be expected that in such a series of salts (with common anion), and in the absence of any specific effect, the valency of the cation would be of prime importance. The position of the H^+ ion in the series appears to be somewhat anomalous, indicating the occurrence of specific adsorption.

Preferential adsorption of a multivalent ion into the Stern layer is shown to a considerable extent in suspensions containing lanthanum chloride, for which the isoelectric point is reached at concentrations approaching 10^{-3}N, the surface thereafter becoming highly positively charged. Owing to the small value of the electrophoretic mobility for particles in suspensions of hydrochloric acid and lanthanum chloride at relatively high concentrations, the accuracy of the measurements is lower than in other cases. However, the ζ-potential is so low at these concentrations that the uncertainty in mobility does not lead to an error in ζ of more than about 1 mv.

In most cases, the charge density bears a linear relation to the cube root of the concentration and at zero concentration the surface charge is zero or very nearly so.

It is noteworthy that this type of relation has been observed before with silica and carborundum surfaces in solutions of acids and salts of various valency types.[18]

Values of A and B (the latter zero unless stated) in the equations $\sigma_2 = 1000AC^{\frac{1}{3}} - B$ governing the adsorption, are:

Gold suspensions: NaOH, A 12·0, B 140; KCl, A 5·4; $BaCl_2$, A 4·6
Silver suspensions: KCl, A 6·85; $BaCl_2$, A 4·2; HCl, A 2·4

Finally these results indicate the non-ionogenic nature of the gold and silver surfaces, since the charge density tends to zero as the bulk ionic concentration approaches infinite dilution.

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Battersea College of Technology, London, S.W.11. [*Received, April 10th*, 1959.]

[18] Benton and Elton, " Proc. 2nd Int. Congr. Surface Activity," Vol. III, Butterworths, London, 1957, p. 28.

776. *Aromatic Sulphonation. Part V.* Kinetic Isotope Effects and Mechanism.*

By J. C. D. Brand, A. W. P. Jarvie, and W. C. Horning.

Indicator measurements are used to obtain values for the autoprotolysis constant of sulphuric acid and the acidity constant of disulphuric acid. It is then shown that h_0 is proportional to the concentration of solvated hydrogen ions, $H_3SO_4^+$, over a considerable section of the range between the compositions H_2SO_4,H_2O and H_2SO_4,SO_3. Activity-coefficient ratios of the form $f_B/f_{H^+}/f_{BH^+}$ appear to be substantially constant in this region. It is therefore suggested that ratios having the more general form $f_X f_Y/f_{XY}$ are also approximately constant in sulphuric acid, and this hypothesis is used to analyse the kinetic dependence of sulphonation on the concentration of the medium in fuming sulphuric acid. Substrate and solvent deuterium isotope effects help to discriminate between possible mechanisms, and it is concluded that the reaction proceeds by stepwise attachment of SO_3 and H^+ to the substrate, followed by the loss of a proton from the benzene ring.

Accumulated evidence [1,2,3] on the mechanism of aromatic sulphonation in sulphuric acid still leaves several points undecided.[4] We try here to settle some of these with the help of new measurements on the kinetic effect of deuterium in the substrate as well as in the sulphonating medium.

(1) *Activity Coefficients in Sulphuric Acid.*—Rate constants for sulphonation in sulphuric acid encompass a profound change of the acid concentration. To give a trustworthy interpretation to the rates it is therefore necessary to have at least a qualitative estimate of the activity-coefficient changes, which otherwise represent an unknown factor in the rate equation. The widespread assumption that activity coefficients are constant in sulphuric acid has been proved inadequate,[5] although variations are less than in aqueous solution. Some activity-coefficient measurements are available in a region close to the composition H_2SO_4 and these will be mentioned later; unfortunately, they do not cover a sufficient range to be of direct application to the kinetics of sulphonation. Further information comes from an analysis of equilibria and this will be the concern of the present section. As the assumption of constant activity coefficients is unsound we take as a working hypothesis the proposition that

$$f_X f_Y/f_{XY} \simeq \text{constant} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

a condition reminiscent of the Zucker–Hammett hypothesis.[6,7] Its status in sulphuric acid is that of an assumption yet to be tested by comparison with experimental data.

Acid–base equilibria in sulphuric acid have been studied extensively.[6,8,9] The formal equation

$$H_2SO_4 \rightleftharpoons H^+ + HSO_4^-; \quad K_S = a_{H^+}\, a_{HSO_4^-}/a_{H_2SO_4} \quad . \quad . \quad . \quad (2)$$

gives [1a]

$$H_0 = pK_S + \log (x_{HSO_4^-}/x_{H_2SO_4}) + \log (f_{BH^+} f_{HSO_4^-}/f_B f_{H_2SO_4}) \quad . \quad . \quad (3)$$

in which x stands for mole fraction. Eqn. (1) gives $f_{BH^+}/f_B \simeq f_{H_2SO_4}/f_{HSO_4^-} \propto f_{H^+}$, and

* Part IV, *J.*, 1952, 3927.

[1] (*a*) Brand, *J.*, 1950, 997; (*b*) Brand, *J.*, 1950, 1004; (*c*) Brand and Horning, *J.*, 1952, 3922.
[2] Gold and Satchell, *J.*, 1956, 1635.
[3] Spryskov, *Zhur. obshchei Khim.*, 1955, **25**, 1731.
[4] Ingold, "Structure and Mechanism in Organic Chemistry," Bell, London, 1953.
[5] Brand, James, and Rutherford, *J.*, 1953, 2447.
[6] Hammett, "Physical Organic Chemistry," McGraw-Hill, New York, 1940.
[7] Long and Paul, *Chem. Rev.*, 1957, **57**, 935.
[8] Paul and Long, *Chem. Rev.*, 1957, **57**, 1.
[9] Brand, Horning, and Thornley, *J.*, 1952, 1374.

hence that the last term in (3) is constant in first approximation. In fact it was shown [1a] that the eqn.*

$$H_0 = -9{\cdot}49 + \log m_{HSO_4^-} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

where $m_{HSO_4^-}$ is the molality of bisulphate ion calculated on the simple assumption that water is quantitatively converted into $H_3O^+HSO_4^-$, gives an excellent account of the experimental H_0 curve in 90—99·5% H_2SO_4 (Fig. 1). [Incidentally, eqn. (1) predicts that H_+, H_0, and H_- will all have the same numerical values in sulphuric acid, and this accords with such facts as are known.[9,10]] Equation (4) can now be used to estimate the bisulphate-ion molality in anhydrous acid ($H_0 = -11{\cdot}12$),[9] and we find $(m_{HSO_4^-})_{m=0} = 0{\cdot}023_4$. Bisulphate ions are formed here by self-dissociation of the solvent to which Gillespie, Hughes, and Ingold [11] attribute the equilibria

$$2H_2SO_4 \rightleftharpoons H_3SO_4^+ + HSO_4^- \text{ (autoprotolysis)} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

$$2H_2SO_4 \rightleftharpoons H_3O^+ + HS_2O_7^- \text{ (ionic dehydration)} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

In anhydrous acid, therefore, $(m_{HSO_4^-})_{m_3=0} = (m_{H_3SO_4^+})_{m_3=0}$ and thus the (mole fraction) autoprotolysis constant, K_{ap}, is $5{\cdot}3 \times 10^{-6}$ at the temperature (20°) of the indicator measurements. Though high, this is consistent with the value $2{\cdot}9 \times 10^{-6}$ (at 20°) derived from thermodynamic measurements by Wyatt and Kirkbride.[12] Another value, K_{ap} (20°) $= 2{\cdot}0 \times 10^{-6}$, can be calculated from Gillespie and Oubridge's data [13] at 10·4° by use of ΔH_{ap}.[12] We do not think that K_{ap} from the indicator experiments is better than the other data (on the contrary, the high value of K_{ap} probably disguises a drift in the ratios $f_X f_Y / f_{XY}$) but the fact that measurements in the range 90—99% H_2SO_4 give a reasonably good picture of the equilibria in anhydrous acid is reassuring evidence that eqn. (1) is valid as a first approximation. Naturally, eqn. (4) would also follow from (3) if all activity coefficients were constant but this, as we shall see, is certainly not correct.

On the fuming side of the composition H_2SO_4 an extra constant is needed to cope with the incomplete ionisation of disulphuric acid. The ionisation is represented by [11]

$$H_2S_2O_7 + H_2SO_4 \rightleftharpoons H_3SO_4^+ + HS_2O_7^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

Eqn. (1) gives $f_{H_3SO_4^+}/f_{H_2SO_4} \simeq f_{H_2S_2O_7}/f_{HS_2O_7^-}$, and thus

$$K_A = x_{H_3SO_4^+} x_{HS_2O_7^-} / x_{H_2S_2O_7} x_{H_2SO_4} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

[The assumption (1) must always eliminate activity coefficients from a "balanced" equilibrium of the form $AB + C \rightleftharpoons AC + B$.] Indicator data in fuming acid are of two sorts. First, one may determine H_0 in presence of a high molality of $HS_2O_7^-$ anions, as when potassium sulphate is dissolved in fuming sulphuric acid. The ions repress the ionic dehydration (6) which can then be ignored. Some results are given in the upper portion of Table 1; they resemble previous data [1a] which, however, are in error to the extent that indicator ratios were determined at a single wavelength, and have therefore been re-evaluated. As autoprotolysis is considerable in sulphuric acid it is necessary to allow for solvolysis of the $HS_2O_7^-$ ion in calculating K_A. The solvolysis has the form

$$HS_2O_7^- + H_2SO_4 \rightleftharpoons H_2S_2O_7 + HSO_4^-; \quad K_H = K_{ap}^*/K_A \quad . \quad . \quad . \quad (9)$$

In Table 1, m_2 and m_3 are respectively the formal molalities of disulphuric acid and hydrogen disulphate ion, calculated on the assumption that the stoicheiometric SO_3 concentration

* 0·12 unit has been subtracted from earlier values [9] of H_0 to render them consistent with Paul's redetermination of the acidity constant of *p*-nitroaniline.[8]

[10] Bonner and Lockhart, *J.*, 1957, 364.
[11] Gillespie, Hughes, and Ingold, *J.*, 1950, 2473; Gillespie, *J.*, 1950, 2493.
[12] Wyatt and Kirkbride, *Trans. Faraday Soc.*, 1958, **54**, 483.
[13] Gillespie and Oubridge, *J.*, 1956, 80.

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equals $m_2 + m_3$. The actual molality of hydrogen sulphate ions (col. 4) is obtained from H_0 by eqn. (4). The requirements of electroneutrality and material balance then give

$$K_A = (K_{ap}/10{\cdot}2)(m_3 + \beta)/(m_2 - \beta)m_{HSO_4} \quad . \quad . \quad . \quad . \quad . \quad (10)$$

where $\beta = m_{H_3SO_4^+} - m_{HSO_4^-}$ is calculable from $m_{HSO_4^-}$ and K_{ap}. This treatment yields the values of K_A given in the final column.

TABLE 1. *Acidity constant of disulphuric acid (nitrobenzene indicator)*

m_2	m_3	$-H_0$	$m_{HSO_4^-}$	β	$K_A \times 10^3$	m_2	$-H_0$	$m_{HSO_4^-}$	β	$K_A \times 10^3$
0·372	0·163	11·44	0·011	0·039	3·0	0·232	11·61	0·0076	0·065	2·8
0·250	0·280	11·17	0·021	0·005	3·1	0·310	11·68	0·0064	0·079	2·9
0·123	0·396	10·87	0·042	−0·029	3·2	0·400	11·74	0·0055	0·095	3·1
0·159	0·101	11·27	0·017	0·016	2·7	0·584	11·82	0·0047	0·113	2·8
0·107	0·151	11·12	0·023	0·000	3·3	0·641	11·84	0·0044	0·122	2·9
0·068	0·205	10·96	0·034	−0·018	3·5	0·747	11·88	0·0041	0·131	2·9
0·160		11·51	0·0095	0·048	2·7	0·855	11·92	0·0037	0·144	3·0

The second series of measurements refers to solutions of disulphuric acid containing no added salt, and appears in the right-hand section of Table 1. Values of K_A in the last column are calculated from eqn. (10) with m_3 set equal to zero. K_A as obtained by this means is described by Gillespie *et al.*[11] as the *apparent ionisation constant* on the ground that disulphuric acid is thought to be in equilibrium with higher polysulphuric acids, but as the evidence for polysulphuric acids is very indirect (at least for dilute oleums) it has been thought unprofitable to refine our calculation at this stage. Gillespie, Hughes, and Ingold express K_A more simply in terms of molalities and obtain, from cryoscopic data, the value $K_A = 0{\cdot}028$ mole kg.$^{-1}$ at 10°. This is clearly consistent with the overall average from Table 1; K_A (20°) $= 3{\cdot}0 \times 10^{-3}$ when the m_1 conversion factor is applied.

Eqns. (2) and (5) give the thermodynamic expression $K_S = K_{ap}\, a_{H^+}\, a_{H_3SO_4^+}/a_{H_4SO_4}$ from which, on introduction of the definition of H_0 [6] as well as the assumption expressed in (1), one finds

$$H_0 = \log K_{ap}/K_S - \log x_{H_3SO_4^+}/x_{H_4SO_4} \quad . \quad . \quad . \quad . \quad . \quad (11)$$

which, on insertion of numerical constants, becomes

$$H_0 = -12{\cdot}75 - \log m_{H_3SO_4^+} \quad . \quad . \quad . \quad . \quad . \quad . \quad (12)$$

The expression (12) includes the previous eqn. (4). The circles in Fig. 1 represent values of H_0 calculated from (12) on the basis of $K_A = 3{\cdot}0 \times 10^{-3}$. On the fuming side, agreement is good for disulphuric acid molalities up to 2 molal and is fair even at much higher molalities. The behaviour that could be implied by Fig. 1, *viz.*, that h_0 is essentially proportional to $m_{H_3SO_4^+}$ between the composition limits $H_2O^+HSO_4^-$ and $H_2S_2O_7$, gives a broad measure of support to the hypothesis represented by (1). It seems improbable that the proportionality would hold so well over so great a range of concentration unless the underlying assumption in regard to the activity coefficients were correct.

When activity coefficients are referred to a standard state in sulphuric acid, eqn. (1) becomes $f_X f_Y / f_{XY} \simeq 1$. As to the individual activity coefficients, however, it is almost certain that they cannot remain at unity. The case of electrolytes has been discussed elsewhere.[5,12] Fig. 2 illustrates the manner of variation for three non-electrolytes in aqueous acid as determined by partition with cyclohexane, that is, from the equation

$$f_B = P/P^\circ \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (13)$$

in which P is the partition coefficient. Evidently a rising molality of water has a salting-out effect, and this appears to be true not merely for the nitro-compounds shown in Fig. 2 but also for small molecules such as SO_2.[14] The changes in f_B need to be kept in perspective moreover. Between 99 and 91·5% H_2SO_4, f_B for 1-chloro-2,4-dinitrobenzene increases

[14] Miles and Carson, *J.*, 1946, 786; Miles and Fenton, *J.*, 1920, **117**, 59.

5-fold whilst the change in h_0 is only 18-fold: thus if the agreement in Fig. 1 is significant, a drift in f_B must be cancelled by an opposite change in f_{H^+}/f_{BH^+}.

One kinetic application of (1) is known to us. If aromatic nitration in sulphuric acid follows a Brønsted rate law, the second-order coefficient, k_2, is given (in the region where $m_{NO_2^+}$ equals the formal nitric acid molality) by

$$k_2 = kf_S f_{NO_2^+}/f_{X^+}$$

in which k is a thermodynamic constant, and S and X denote substrate and transition state. k_2 for nitration of the *p*-bromophenyltrimethylammonium ion is given in Table 2. Were

TABLE 2. *Nitration of* p-*bromophenyltrimethylammonium ion* (25°).

Free SO_3 (%)	0·00	1·29	7·38	14·1	18·6	22·2
$k_2 \times 10^3$	2·79	2·90	3·54	4·68	4·85	4·67

(1) to hold rigorously, k_2 would be independent of the composition of the medium; the actual variation is less than 2-fold. (On the aqueous side the variation is somewhat

FIG. 1. *The limits of the concentration range correspond to the compositions* H_2SO_4,H_2O *and* H_2SO_4,SO_3.

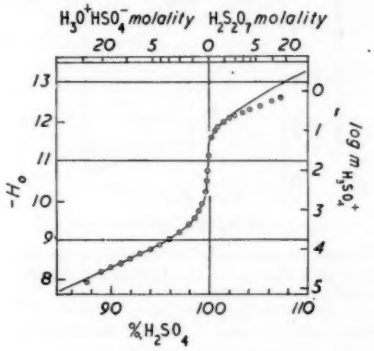
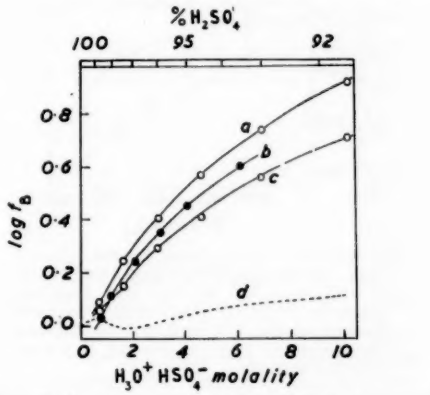


FIG. 2. *Activity coefficients of some non-electrolytes in* H_2SO_4 (20°).



a, *p*-Chloronitrobenzene. *c*, 1-Chloro-2,4-dinitrobenzene.
b, Nitrobenzene. *d*, Sulphur dioxide.[14]

larger, 2·5-fold between 94·7 and 100% H_2SO_4.[15]) Although the quality of the approximation $f_S f_{NO_2^+} \simeq f_{X^+}$ is only fair in this instance, there are no large effects due to the medium left unexplained.

(2) *Kinetic Effect of Deuterium on the Rate of Sulphonation.*—In fuming sulphuric acid, reaction conditions can be adjusted so that the sulphonation rate greatly exceeds the rate of deuterium exchange between substrate and solvent. Thus a kinetic isotope effect can be observed on one hand by substituting deuterium in the substrate, and on the other by substitution in the sulphonating medium.

Berglund-Larsson and Melander [16] determined the kinetic effect of deuterium in the substrate for the sulphonation of [4-^{2}H]- and [4-^{3}H]-bromobenzene in a mixed solvent of nitrobenzene and oleum. The effect found was small ($k_D/k_H = 0·7$) and lacked any significant variation with temperature. These conclusions are confirmed by the present measurements (Table 3), which also show that k_D/k_H is insensitive to the composition of the sulphonation medium.

[15] Bonner, Bowyer, and Williams, *J.*, 1952, 3274; *J.*, 1953, 2650.
[16] Berglund-Larsson and Melander, *Arkiv Kemi*, 1953, **6**, 219; Berglund-Larsson, *ibid.*, 1957, **10**, 549.

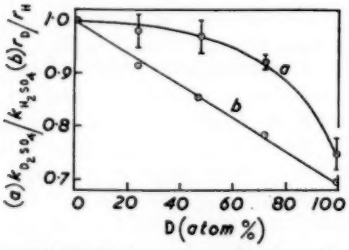
TABLE 3. *Kinetic effect of deuterium substitution in the substrate.*

	Substrate:		*p*-X·C_6H_4·NMe_3^+			C_6H_5·NO_2 [a]
	Medium:	X = CH_3	X = F	X = Cl	X = Br	
Temp.	free SO_3 (%)			k_D/k_H (±0·03)		
0°	11·6	$0·54_7$	—	—	—	—
25	11·6	$0·57_7$	—	—	—	—
25	14·3	—	—	—	—	0·59
25	22·2	$0·57_7$	—	—	—	0·60
25	35·3	—	$0·49_6$	$0·48_4$	$0·51_1$	0·63
25	42·7	—	$0·48_1$	$0·50_8$	$0·50^b$ / $0·52_4$	—

[a] Substrate, 5×10^{-4}M. [b] Substrate, 0·01M. Otherwise the substrate concn. was 0·15—0·3M.

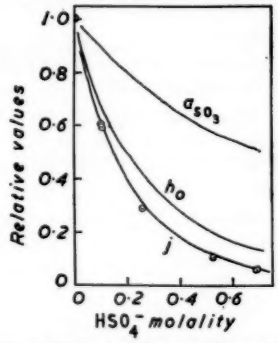
The kinetic effect of deuterium substitution in the solvent can be seen from Fig. 3. The measurements refer to a changing proportion of deuterium in a fuming acid medium of otherwise constant composition: the effect then represents a slight retardation, with

FIG. 3. *Effect of solvent deuterium: sulphonation rates* (25°, *curve a*) *and indicator ratios* (20°, *curve b*).



The ordinate is $k_{D_2SO_4}/k_{H_2SO_4}$ for the velocity data (*p*-Me·C_6H_4·NMe_3^+ ion), and r_D/r_H ($r = c_{base}/c_{ion}$) for the indicator measurements (*m*-F·C_6H_4·NO_2 indicator). The mole fraction of free SO_3 is 0·0857 throughout (equivalent to 7·1% of free SO_3 in a non-enriched solvent).

FIG. 4. *Effect of hydrogen disulphate ion on the rate of sulphonation* (25°).



The curves connect relative values of a_{SO_3}, h_0, and *j* with the moles of hydrogen sulphate ion added (as potassium sulphate) to 1 kg. of a solvent containing 15·6% of free SO_3. The points are relative rate constants for the trimethylphenylammonium ion.[15]

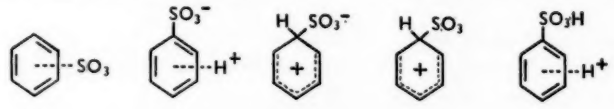
$k_{D_2SO_4}/k_{H_2SO_4} = 0·7_5$. Under the chosen conditions no deuterium was introduced into the substrate during reaction. Fig. 3 also shows the influence of solvent deuterium on the ionisation ratio, $r = c_B/c_{BH^+}$, of the indicator *m*-fluoronitrobenzene. Enrichment increases the proportion of the conjugate acid of the indicator, a change which is in the same sense as that observed for (weak) acids in aqueous solution.[17,18] No other photometric measurements seem to have been made in fuming acid, though Schubert and Burkett [19] record $r_D/r_H = 0·44$ for mesitaldehyde in 59—70% H_2SO_4. (Flowers, Gillespie, and Oubridge,[20] however, report conductometric measurements for *m*-nitrotoluene in anhydrous D_2SO_4 which imply *less* ionisation than in H_2SO_4. The relation of this to the photometric results stands unexplained.)

(3) *Kinetic Dependence of Sulphonation Rate on Acidity.*—Sulphonation rates in sulphuric acid are of apparently first order (k_1). In fuming acid, it was noted earlier [1] that log k_1 varies almost linearly with $-H_0 + \log a_{SO_3}$ ($\equiv -J$), the slopes ranging from 1·0 to 1·2 for different substrates, over a 5000-fold change in k_1. Likewise, the results in Fig. 4 show that sulphonation rates in presence of potassium sulphate correlate with j(= −antilog J)

[17] Wiberg, *Chem. Rev.*, 1955, **55**, 713.
[18] Bell, "Acid-Base Catalysis," Oxford Univ. Press, London, 1949.
[19] Schubert and Burkett, *J. Amer. Chem. Soc.*, 1956, **78**, 64.
[20] Flowers, Gillespie, and Oubridge, *J.*, 1958, 667.

rather than with h_0 or a_{SO_3}. The inference is then that a proton and an SO_3 molecule attach to the substrate in the transition state. However, in view of evidence that sulphur trioxide (or its dimer) is an effective agent in aprotic solvents.[4,21] it is necessary to consider whether the correlation is significant, or whether the changing medium merely affects k_1 in a manner that happens to lead to the parallelism with $-J$. Experiments in aqueous acid have recently been interpreted in favour of a transition state containing SO_3 only in addition to the substrate, rather than $SO_3 + H^+$.[2]

In view of the isotopic measurements, three mechanisms need consideration. The first is that developed by Gold and Satchel [2] for aqueous acids. These authors consider



(I) (II) (III) (IV) (V)

that rearrangement of the non-classical structure (I) to the corresponding structure (II), probably by way of the Wheland intermediate (III), is rate-controlling. Their mechanism is then,

$$ArH + SO_3 = ArH,SO_3 \text{ (I)} \quad \text{(Fast) (A)}$$

$$ArH,SO_3 = ArSO_3^-,H^+ \text{ (II)} \quad \text{(Slow) (B)}$$

$$ArSO_3^-,H^+ = ArSO_3^- + H^+ \quad \text{(Fast) (C)}$$

The Brønsted rate eqn. gives

$$v/[ArH] = k_1 = Ab.a_{SO_3}.f_{ArH}/f_X \quad (14)$$

in which A denotes the equilibrium constant for (A), and b the thermodynamic rate constant for step (B). Introducing (1) in the form $f_{ArH}f_{SO_3} \simeq f_X$, we find

$$k_1 = Ab.a_{SO_3}/f_{SO_3} \quad (15)$$

a_{SO_3} can be identified with the vapour pressure of sulphur trioxide. Because of the range of rates, eqn. (15) is more clearly tested by logarithmic graphs. Curve I, Fig. 5, is a plot of log k_1 against log a_{SO_3}; [21] the graph is not linear and has the further implication that, if eqn. (15) is valid, f_{SO_3} must decrease about 65-fold in the range of acid composition encompassed by the Figure (101—109% H_2SO_4). Likewise, the results in Fig. 4 imply that f_{SO_3} also decreases with electrolyte concentration (" salting-in "), whereas salting-out would have been expected owing to the increasing ionic strength (cf. Section 1). Although f_{SO_3} is not known, it would be plausible to assume that its variation is like that of f_{SO_3}, which decreases 2-fold in the region 101—109% H_2SO_4.[14] While this mechanism cannot be ruled out, it does not seem adequately to express the sulphonation rates in fuming acid.

The second mechanism is one of attack by SO_3H^+,[1]

$$SO_3 + H^+ = SO_3H^+ \quad \text{(Fast) (D)}$$

$$ArH + SO_3H^+ = Ar\begin{matrix}H\\SO_3H\end{matrix} \text{ (IV)} \quad \text{(E)}$$

$$Ar\begin{matrix}H\\SO_3H\end{matrix} = ArSO_3H,H^+ \text{ (V)} \quad \text{(F)}$$

The rearrangement of a Wheland intermediate (IV) to the non-classical structure (V) is regarded as rate-controlling, although variants are possible. [In Part III [1c] the step (E) was erroneously taken to be rate-controlling; this is not consistent with a substrate deuterium effect.] This mechanism leads to a rate equation of the correct form, but is unacceptable on other grounds. The indicator measurements imply that SO_3D^+ in

[21] Vicary and Hinshelwood, *J.*, 1939, 1372; Wadsworth and Hinshelwood, *J.*, 1944, 469; Dresel and Hinshelwood, *J.*, 1944, 649.

D_2SO_4 should be more abundant than SO_3H^+ in H_2SO_4, and therefore that the rate should increase in a deuterium solvent. The observations show a decrease of rate (Fig. 3). Although it is conceivable that the expected, small increase has been cancelled by, for example, an effect of the medium accompanying deuterium substitution in the solvent, yet the data evidently contain no support for the mechanism.

The third mechanism differs chiefly in its estimate of the timing. SO_3 and H^+ may add to the substrate consecutively: then one has,

$$ArH + SO_3 = Ar\begin{matrix}H\\SO_3\end{matrix} \quad (III) \quad \ldots\ldots\ldots \quad (Fast)\ (G)$$

$$Ar\begin{matrix}H\\SO_3\end{matrix} + H^+ = Ar\begin{matrix}H\\SO_3H\end{matrix} \quad (IV) \quad \ldots\ldots\ldots \quad (H)$$

$$Ar\begin{matrix}H\\SO_3H\end{matrix} = ArSO_3H,H^+ \quad \ldots\ldots\ldots\ldots \quad (F)$$

Here the intermediate (III) is considered to accept a proton before the final, non-reversing

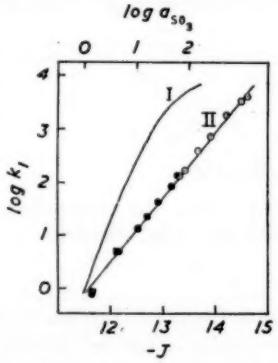


FIG. 5.

Curve I (individual points not shown): log k_1 *against* a_{SO_3}.

Curve II: log k_1 *against* $-J$. ●, $C_6H_5{\cdot}NMe_3^+$; □, p-$Me{\cdot}C_6H_4{\cdot}NMe_3^+$, log $k^1 - 2{\cdot}56$; ⊙, p-$F{\cdot}C_6H_4{\cdot}NMe_3^+$, log $k_1 + 1{\cdot}81$.

step (F). The form attributed to the reversible step (H) merely recognises that the approximation (1), which is implied throughout the analysis, means that the reaction

$$Ar\begin{matrix}H\\SO_3\end{matrix} + H_3SO_4^+ = Ar\begin{matrix}H\\SO_3H^+\end{matrix} + H_2SO_4$$

leads to the same rate equation as its formal representation (H). Taking (G) as a pre-equilibrium, applying the stationary-state hypothesis to the concentration of (IV), and introducing the simplifying assumption (1), we obtain the rate equation,

$$k_1 = Gf\frac{h_+}{h_- + f}h_0 a_{SO_3}/f_{SO_3} \quad \ldots\ldots\ldots \quad (16)$$

in which h_+ and h_- are rate constants for the forward and the reverse step (H). The scheme (D, E, F) when treated likewise gives an equation of the same form, namely,

$$k_1 = Df\frac{e_+}{e_- + f}h_0 a_{SO_3}/f_{SO_3} \quad \ldots\ldots\ldots \quad (17)$$

Both mechanisms predict, therefore, that the graph of log k_1 against $-J[= \log(h_0 \times a_{SO_3})]$ should have a slope in excess of 1·0, because f_{SO_3} is expected to rise with oleum concentration. This, however, is a somewhat naïve explanation of the observed slope of 1·2 (Fig. 5), for the expressions (16) and (17) involve the hypothesis (1) and must be in error to the extent that this approximation fails.

Whereas deuterium can be expected to retard a reaction involving proton transfer by

a factor of 2½—10, the results for the *m*-fluoronitrobenzene indicator imply that a pre-equilibrium involving proton transfer will lead to acceleration in the deuterium solvent by a factor up to 1·4. These factors being descriptively called large and small respectively,

TABLE 4.

p-X·C_6H_4·NMe_3^+	Medium: free SO_3 (%)	F_D of isolated product max.	obs.	p-X·C_6H_4·NMe_3^+	Medium: free SO_3 (%)	F_D of isolated product max.	obs.
X = CH_3	2·09	1·40	0·090	X = F	35·7	1·80	(0·019)
CH_3	4·53	1·48	0·038	Cl	35·7	1·80	(0·023)
CH_3	8·00	1·52	(0·018)	Br	35·7	1·80	(0·021)

TABLE 5.

Mechanism	Limit	Description	First-order kinetic effect of D in: Solvent	Substrate
(D, E, F)	$e_- \gg f$	(E) pre-equilibrium	small increase	large decrease
(G, H, F)	$h_- \gg f$	(H) pre-equilibrium		
(D, E, F)	$e_- \ll f$	(E) non-reversing	small increase	none
(G, H, F)	$h_- \ll f$	(H) non-reversing	large decrease	none

Table 5 summarises the predictions of the last two mechanisms under limiting conditions. For instance, when $h_- \ll f$ the right-hand side of (16) becomes $Gh_+ h_0 a_{SO_3}/f_{SO_3}$, and thus the scheme (G, H, F) predicts that solvent deuterium will bring about a large decrease in rate owing to the isotope effect on the coefficient h_+. It is worth noting that in the limits $e_- \gg f$ and $h_- \gg f$ [when (E) and (H) are pre-equilibria in their respective mechanisms] the mechanisms are not distinguishable kinetically, for the rate-controlling step is then the rearrangement of the intermediate (IV) whose concentration is unaffected by the order of previous events.*

One aspect of the Table is that, as noted earlier, the scheme (D, E, F) cannot be reconciled with the observed retardation by solvent deuterium, since the limiting situations correspond to an unchanged rate and a small acceleration. Thus we feel bound to discard SO_3H^+ as the sulphonating species in oleum. The scheme (G, H, F) is acceptable, however, because the predicted effect of solvent deuterium ranges from a large decrease to a small increase, while that for solute deuterium extends from no effect to a large decrease. Therefore an intermediate situation, in which h_- and f are to be thought of as being of the same order of magnitude, may well yield the observed low-order retardation by both solvent and solute deuterium. Physically, the the reaction intermediate (IV) may lose either nuclear hydrogen (giving rise to sulphonation) or hydrogen from the sulphonic acid group [regenerating the intermediate (III)], these two events having roughly equal probability. On general grounds, the loss of a nuclear proton from (IV) will certainly occur more readily than from (III), and this may be important for the relatively difficult sulphonations studied in fuming acid. Moreover, the electronic demand of a substituent in the aromatic nucleus affects the coefficients h_- and f in the same sense, and hence the balance between them need not be disturbed when one substituent is replaced by another.

An alternative to the unimolecular step (F) is

$$Ar\begin{matrix}H\\SO_3H^+\end{matrix} + H_2SO_4 = Ar{\cdot}SO_3H + H_3SO_4^+ \quad \ldots\ldots\ldots \quad (F')$$

in which the proton is transferred directly to the solvent without the intervention of a non-classical structure. The criteria used in this paper do not distinguish (F) and (F'). (F) has been used in the foregoing discussion only because the balance of evidence from desulphonation [2] appears to favour a mechanism of this kind.

EXPERIMENTAL

Deuterium Analysis.—Sufficient organic compound to provide about 50 mg. of water was burnt in a standard semimicro-combustion apparatus. The water was purified by refluxing

* We thank a Referee for drawing attention to this point.

over alkaline potassium permanganate [24] and degassed by several distillations *in vacuo*. Deuterium was determined, essentially as described by Gaunt,[25] from the intensity of infrared absorption at 4·03 μ. The cells used were of thin silica, their depth being 0·23 mm. for estimations in the range (0·3—0·8 atom % D) usually employed. The atom % D ($\equiv F_D$) is quoted (Table 4) relative to the natural abundance and is based on the manufacturer's analysis (99·75% w/w) of deuterium oxide. In the range $0·3 < F_D < 0·8$, individual analyses were reliable to ±0·005, the mean deviation being ±0·003%. However, at very low enrichments the method gave erroneously high results; for instance, combustion of unenriched compounds tended to give water with an apparent F_D of ≤0·02. Attempts to remove this discrepancy, attributed to the " memory " of the combustion train, were unsuccessful. Enrichments of this order could not be obtained reliably, or even distinguished from zero.

Sulphonation Media.—The concentration of fuming acid media was controlled by water-titration and conductivity measurements.[9] Partially deuterated acids were prepared by dilution of a more concentrated medium with deuterium oxide. Fully deuterated media ($F_D = 99·7$) were obtained by slowly distilling sulphur trioxide *in vacuo* into deuterium oxide at 0°, the composition being calculated from the vacuum-corrected masses of the components.

Preparation of Derivatives of Methyl [3-^{2}H]*Phenyltrimethylammonium Sulphate.*—No attempt was made to replace nuclear hydrogen quantitatively by deuterium, and substrates studied in sulphonation usually had $F_D = 0·3$—0·5. If necessary, deuterated material was recrystallised with light compound to bring the enrichment down into this range.

Methyl [3-^{2}H]4-*methylphenyltrimethylammonium sulphate.* 5-Amino-2-methylphenyllithium was decomposed with deuterium oxide, and the product fractionally distilled to yield [3-^{2}H]4-methylaniline which was converted into the quaternary salt by standard procedure.[1b] Freedom from unwanted [2-^{2}H]4-methylaniline was established by bromination of the base ($F_D = 0·385$) to [3-^{2}H]2,6-dibromo-4-methylaniline ($F_D = 0·502$). If deuterium is present exclusively in the 3-position the ratio of the enrichments is 9/7 = 1·286, the observed ratio being 1·30 ± 0·03.

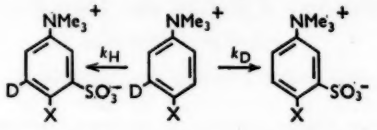
[3-^{2}H]4-*Fluoro-*, [3-^{2}H]4-*chloro-, and* [3-^{2}H]4-*bromo-phenyltrimethylammonium methyl sulphates.* Preliminary experiments indicated that deuterium could be introduced conveniently into *p*-nitroacetanilide by treatment with an enriched sulphuric acid–water mixture (0·52 mole fraction of H_2SO_4) at 20°. The components were shaken for several hours, the *p*-nitroacetanilide was hydrolysed, and the resulting *p*-nitroaniline recrystallised from water to displace all deuterium linked to nitrogen, and analysed isotopically. The treatment introduced deuterium in the 2- and 3-positions, though about 95% of the exchange occurred in the latter. This was demonstrated by several experiments of which the following is typical. [2,3-^{2}H]4-Nitroaniline ($F_D = 1·06$) was diazotised and converted into *p*-chloronitrobenzene by the Sandmeyer method, and then hydrogenated in ethanol over Raney nickel to *p*-chloroaniline ($F_D = 1·02$). As deuterium *ortho* to an amino-group is known to exchange over Raney nickel,[26] the 0·04 atom % of D lost in this process is that originally present as [2-^{2}H]4-nitroaniline. The inference that hydrogenation yielded [3-^{2}H]4-chloroaniline was confirmed by bromination of a sample in methanol to give [3-^{2}H]2,6-dibromo-4-chloroaniline, $F_D = 1·53$ (calc., 1·53). The [3-^{2}H]-chloroaniline was then converted into [3-^{2}H]4-chlorophenyltrimethylammonium methyl sulphate by the method previously described.[1c] Similar reactions were used to prepare [3-^{2}H]4-fluorophenyltrimethylammonium methyl sulphate.

In another series of experiments [2,3-^{2}H]4-nitroaniline was diazotised and reduced to [2,3-^{2}H]nitrobenzene by treatment with hypophosphorous acid at 0°. Catalytic hydrogenation (Raney nickel) then gave [3-^{2}H]aniline which on bromination in acetic acid yielded [3-^{2}H]-bromoaniline. [3-^{2}H]4-Bromophenyltrimethylammonium methyl sulphate was obtained from the amine by quaternisation in the usual way.[1c]

Kinetic Effect of Nuclear Deuterium.—The relative velocities of displacement of nuclear hydrogen and deuterium were determined competitively. Sulphonation of a quaternary ion of the type (VI) yields a product isolable as the dipolar ion (VII) or (VIII). The results, given in Table 3, are the average of two or more concordant experiments. The uncertainty attached

[22] Brand and Rutherford, *J.*, 1952, 3916.
[23] Brayford and Wyatt, *J.*, 1955, 3453.
[24] Keston, Rittenberg, and Schonheimer, *J. Biol. Chem.*, 1937, **122**, 227.
[25] Gaunt, *Spectrochim. Acta*, 1956, **8**, 57.
[26] Lauer and Errede, *J. Amer. Chem. Soc.*, 1954, **76**, 5162.

there to k_D/k_H is based on a limit of error of $\pm 0{\cdot}005$ in F_D. Sulphonation of the aryltrimethylammonium ions was allowed to run for ten half-lives of the reaction at a fixed temperature



(VII) (VI) (VIII)

(usually 25°). The solution was then diluted with water, neutralised with barium carbonate, and concentrated to small volume, any barium remaining in solution [mainly as $Ba(SO_4Me)_2$] then being precipitated with the correct quantity of sulphuric acid. Evaporation at reduced pressure gave a residue of the trimethyl-3-sulphoarylammonium betaine (VII) or (VIII) which was recrystallised once from aqueous alcohol. The isotope analyses were erratic if crystallisation was omitted, probably owing to occlusion of methyl hydrogen sulphate.

The calculation of k_D/k_H assumes no exchange between nuclear deuterium and sulphuric acid and would fail to the extent that this assumption is invalid. As deuterium exchange is electrophilic in character, it was expected that exchange would affect the substrate (VI) rather than the product and that it would most likely be observed with the *p*-tolyl compound (VI; X = Me). Table 4 summarises tests in which non-enriched aryltrimethylammonium methyl sulphate was sulphonated with acid containing deuterium: col. 3 gives the value of F_D expected if partition of deuterium between solvent and substrate (3-position) had reached equilibrium, while col. 4 cites the enrichment observed. As mentioned earlier, apparent enrichments of $F_D \leqslant 0{\cdot}025$ are certainly too high and may well correspond to $F_D = 0$. The results show that exchange is inappreciable relative to the rate of sulphonation, except in media of low sulphur trioxide concentration. Separate experiments confirmed that non-enriched betaines recovered from solution in a deuterium solvent had not undergone significant exchange.

Experiments with nitrobenzene were made with a sample of pentadeuteronitrobenzene kindly supplied by Dr. T. Bonner and Professor G. Williams.[15] Here, rate constants were determined separately for the light and heavy compounds by the method described earlier.[1c]

Kinetic Effect of Deuterium in the Sulphonation Medium.—The effect of deuterium as solvent was measured for the sulphonation of (non-enriched) methyl *p*-tolyltrimethylammonium sulphate in enriched acid containing *ca.* 7·1% of free sulphur trioxide. The substrate does not exchange in this medium (cf. Table 4) and thus the results refer to sulphonation of unenriched substrate by enriched acid. Rate constants were determined as described previously,[1c] and the isotope effect is expressed by the ratio, $k_{D_2SO_4}/k_{H_2SO_4}$, of the first-order rate coefficients in enriched and non-enriched acids of the same molar composition.

Nitration of Methyl p-*Bromophenyltrimethylammonium Sulphate.*—The substrate (*ca.* 10^{-3}M initially) was nitrated in a solution of potassium nitrate (0·1M) in fuming sulphuric acid, progress of the reaction being followed photometrically (at 365 mμ). The first-order rate observed is the sum of the rate constants for nitration and sulphonation. Subtraction of the rate constant for sulphonation (significant in the stronger acids only) gave the first-order constant for nitration, which was expressed as a second-order constant (k_2, Table 2) by dividing by the formal nitric acid concentration.

Indicator Measurements.—Ionisation ratios, *r*, for the indicator *m*-fluoronitrobenzene were measured [9] in relation to the deuterium content of the medium in an acid of the same composition (7·1% of free SO_3) as that used to determine the kinetic effect of solvent deuterium.

Partition Experiments.—5 ml. of a solution of the non-electrolyte in cyclohexane were shaken for 15 min. with an equal volume of sulphuric acid at 20° (equilibration required 3—8 min.), and the concentration in each of the separated phases was then determined spectrophotometrically. In some experiments the relative volumes of the two phases were altered: this had no observable effect on the constancy of the partition coefficient, *P*.

We thank Dr. G. Eglinton and his staff for advice on deuterium analyses. One of us (A. W. P. J.) is indebted to D.S.I.R. for a maintenance allowance.

THE UNIVERSITY, GLASGOW, W.2. [*Received, April 24th*, 1959.]

777. *The Common-ion Effect in the Unimolecular Solvolysis of t-Butyl Chloride.*

By C. A. Bunton and B. Nayak.

The solvolysis of t-butyl chloride in aqueous methanol is accompanied by exchange of chloride between it and radioactive chloride ion. This exchange is apparently not an S_N2 reaction between chloride ion and alkyl chloride, but is caused by capture of some of the carbonium ions by chloride ions instead of by water. This intervention by chloride ions is compared with that by azide ions.

The classical work on the solvolysis of t-butyl chloride provided one of the earliest examples of an S_N1 reaction.[1] The carbonium ion so formed would be expected to be short-lived, and the hydrolysis of optically active 3-chloro-3,7-dimethyloctane (which is structurally similar to t-butyl chloride) gives an alcohol of inverted configuration, with *ca.* 80% loss of optical activity.[2] Thus the carbonium ion is captured by water molecules before it attains its most stable, planar configuration. Somewhat similarly the product of methanolysis of the hydrogen phthalate of 3,5-dimethylhexan-3-ol has an inverted configuration, with appreciable racemisation.[3]

It has been suggested that the solvolysis of t-butyl chloride in aqueous ethanol should be taken as an example of a limiting S_N1 reaction, and its rate has been taken as a standard in setting up a scale of ionising power for a variety of solvents.[4] The relations between solvent composition and both products and reaction rates have been studied in great detail.[5]

Alkyl halides, *e.g.*, diphenylmethyl chloride, which give comparatively stable carbonium ions, show a characteristic kinetic retardation of solvolysis by the common (chloride) ion, because the carbonium ion (R^+) may react either with this, to regenerate the alkyl halide, or with the solvent:[6]

$$R\text{-}Cl \underset{+Cl^-}{\overset{-Cl^-}{\rightleftharpoons}} R^+ \xrightarrow{H_2O} R\text{-}OH + H^+$$

This retardation has not been observed in hydrolyses of t-alkyl halides. This may be simply because the retarding effect of the common ion was obscured by the acceleration due to increase in the ionic strength. There was an indication, from a decrease of the rate constant in the latter part of the reaction of t-butyl chloride, that such an effect was only just outside the limits of detection, and there was strong evidence of an effect of azide upon the carbonium ion.[1b] It was, however, possible that there was some real mechanistic difference between the solvolyses of t-alkyl halides and of, *e.g.*, diarylmethyl halides. Our work was designed to avoid this difficulty by using an isotopic tracer to prove incorporation of chloride ions into the unhydrolysed t-butyl chloride and to show that this was not a bimolecular reaction between chloride ions and t-butyl chloride itself.

t-Butyl chloride was allowed to hydrolyse in alkaline aqueous methanol containing $Na^{36}Cl$ in several-fold excess over the alkyl halide. After a time sufficient for partial reaction, the t-butyl chloride, with other volatile substances, was pumped off, and its

[1] (*a*) Hughes, *J.*, 1935, 255; (*b*) Bateman, Hughes, and Ingold, *J.*, 1940, 960; Bateman, Church, Hughes, Ingold, and Taher, *J.*, 1940, 979.
[2] Hughes, Ingold, Martin, and Meigh, *Nature*, 1950, **166**, 679.
[3] Doering and Zeiss, *J. Amer. Chem. Soc.*, 1953, **75**, 4733.
[4] Grunwald and Winstein, *ibid.*, 1948, **70**, 846.
[5] (*a*) Olson and Halford, *ibid.*, 1937, **59**, 2644; Speith, Ruelesamen, and Olson, *ibid.*, 1954, **76**, 6253; Speith and Olson, *ibid.*, 1955, **77**, 1412; (*b*) Bateman, Hughes, and Ingold, *J.*, 1940, 881.
[6] Ingold, "Structure and Mechanism in Organic Chemistry," Bell, London, 1953, p. 360.

specific activity determined. All the exchange experiments were made with alkali in excess over t-butyl chloride to eliminate chloride exchange *via*:

$$Me_3C{\cdot}OH + HCl \rightleftharpoons Me_3CCl + H_2O$$
$$Me_2C{:}CH_2 + HCl \rightleftharpoons Me_3Cl$$

(cf. exchange between t-butyl chloride and hydrogen chloride in formic acid [7]). Control experiments were done to ensure that (*a*) no chloride ion came over as a spray in the distillate, and (*b*) a representative sample of t-butyl chloride was pumped over (see p. 3857).

Results of these exchange experiments are given in Table 1; the ratio $k_E/(k_E + k_O)$ gives the proportion of carbonium ions which are captured by chloride ions and regenerate t-butyl chloride. The rates of solvolysis are given in Table 2. The amount of olefin elimination was measured (see p. 3857); it is similar to that found in other solvents. The kinetic form also is similar to that found for other solvents, and added salts increase the rate. Lyate ions (OH^- and OMe^-) have little effect (see ref. 8).

TABLE 1. *Isotopic exchange between chloride ions and t-butyl chloride.* 35·0°. [Bu^tCl] ≈ 0·085M. Methanol–water 80 : 20 (v/v).

[NaCl] (M)	[NaN_3] (M)	Exchange (%) †	$\frac{k_E}{k_E + k_O}$
0·30	—	6·0 (5·9) at 50% reaction	0·09
,,	—	10·9 (11·0) at 75% reaction	0·07
Methanol–water 75 : 25 (v/v)			
0·50	—	7·1 (6·9) at 50% reaction ‡	0·1
,,	—	14·4 (13·4) at 75% reaction	0·1
0·25	0·25	4·4 at 53% reaction	0·06
,,	,,	8·5 at 75% reaction	0·06
,, *	0·75	3·1 (2·6) at 50% reaction	0·04
,, *	,,	6·4 at 75% reaction	0·04

* LiCl. † The figures in parentheses are for redistilled samples.
‡ With reagent concentration as used here, n-butyl chloride gave <0·1% exchange in 65 min.

TABLE 2. *First-order rate constants of solvolysis in aqueous methanol.* [Bu^tCl] ~ 0·085M. Methanol–water 80 : 20 (v/v).

Reagent	—	NaCl		NaOH
[Reagent] (M)	—	0·25	0·50	0·118
10^5k_1 (sec.$^{-1}$) 25·0°	2·12	2·48	2·64	2·19
10^5k_1 (sec.$^{-1}$) 35·0°	7·45	8·55	9·35	7·78

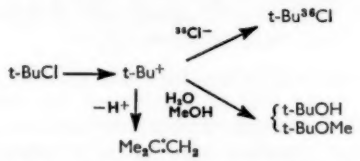
Methanol–water 75 : 25 (v/v) Reagent		NaCl		NaOH	NaOH	NaCl
[Reagent] (M)	—	0·25	0·50	0·112	0·097	0·50
10^5k_1 (sec.$^{-1}$) 25·0°	4·25	4·68	5·06	4·30	—	
10^5k_1 (sec.$^{-1}$) 35·0°	14·7	16·6	17·9	14·7	17·7	

Reagent	NaN_3	NaOH	NaN_3	LiOH	LiCl	NaN_3
[Reagent] (M)	0·50	0·095	0·50	0·112	0·25	0·75
10^5k_1 (sec.$^{-1}$) 25·0°	—	—		—		
10^5k_1 (sec.$^{-1}$) 35·0°	22·4	22·5		23·7		

It could reasonably be suggested that this exchange is a bimolecular reaction between t-butyl chloride and chloride ions, but this is most unlikely, because n-butyl chloride does not exchange its chlorine under conditions in which t-butyl chloride does, and a primary is much more reactive than a tertiary alkyl halide by the S_N2 mechanism. Also the bimolecular exchange between halide ions and a tertiary alkyl halide in acetone is very slow, and from this, and the known effect of solvent changes upon the rates of S_N2 reactions,

[7] Koskoski, Thomas, and Fowler, *J. Amer. Chem. Soc.*, 1941, **63**, 2451.
[8] Benfey, Hughes, and Ingold, *J.*, 1952, 2494.

we can be reasonably certain that there is no such bimolecular exchange in the conditions of our experiments.[9] Thus the mechanism of exchange must be:



In this representation it is not suggested that the t-butyl carbonium ion has attained its most stable, planar, configuration before its capture, because the solvolysis product of a structurally similar optically active compound is not racemic.[2] This can be considered as a " shielding " by the departing ion.[10] It could also be explained in terms of Winstein's ion-pair hypothesis,[11] although the present evidence for such intermediates comes from reactions carried out in solvents of low dielectric constant.

The exchange experiments show that with [chloride ion] = 0·5M about 10% of the carbonium ions (or ion pairs) return to t-butyl chloride, and, with the results of the stereochemical experiments, they show that these ions are not captured immediately by the adjacent water molecules, but exist for a time sufficient for approach of the common (chloride) ion. The experiments are therefore very similar in scope to those on the oxygen exchange and racemisation of secondary alcohols in acid.[12]

With t-butyl chloride the extent of common-ion intervention is small, relative to that for diarylmethyl halides, but it is generally found that the most reactive species will discriminate least towards reagents. Thus the reactive t-butyl carbonium ion will be captured preferentially by the most abundant reagent, *i.e.*, the solvent molecules.

These interventions by chloride, in the hydrolysis of t-butyl chloride, are similar to those of azide ions, and it is possible to carry out a competition experiment between azide and chloride ions. Addition of azide ions decreases the extent of chloride exchange. The effect is small (Table 1), and large concentrations of azide were used; this is because with t-butyl chloride the extent of anion intervention is itself small. From these experiments we calculate the extent of carbonium ion capture by chloride and azide ions. In methanol–water (75 : 25 v/v), 0·5M-chloride ions capture *ca.* 10% of the carbonium ions, whereas the same concentration of azide ion captures *ca.* 13% (Tables 1 and 3). The extent of intervention by azide ions is similar to that observed for other solvolyses of t-butyl halides.[1b]

TABLE 3. *Intervention by azide ion.*

Solvent: Methanol–water 75 : 25 (v/v). 35·0° [t-BuCl] ≈ 0·085M.

[NaOH] (M)	—	—	0·10	0·10	0·113 *
[LiCl] (M)	—	—	—	—	0·25
[NaN_3] (M)	0·50	1·00	0·50	1·00	0·75
Yield of Bu^tN_3 (mole %)	13·4	22·6	11·8	19·7	17·0

* LiOH.

EXPERIMENTAL

Materials.—t-Butyl chloride (B.D.H.) was distilled, and a sample with b. p. 51° collected. Methanol was dried by distillation over magnesium. Sodium and lithium chlorides were oven-dried at 250°. Sodium [^{36}Cl]chloride was prepared by neutralisation of H^{36}Cl with sodium hydroxide. Sodium chloride solution was then added to give radioactive sodium chloride of the required activity; this was purified by recrystallisation from water and oven-dried at

[9] de la Mare, Fowden, Hughes, Ingold, and Mackie, *J.*, 1955, 3200.
[10] Hughes, Ingold, and Masterman, *J.*, 1937, 1196.
[11] Fainberg and Winstein, *J. Amer. Chem. Soc.*, 1956, **78**, 2763, and accompanying papers.
[12] Bunton, Konasiewicz, and Llewellyn, *J.*, 1955, 604; Bunton and Llewellyn, *J.*, 1957, 3402; Bunton, Llewellyn, and Wilson, *J.*, 1958, 4747; Grunwald, Heller, and Klein, *J.*, 1957, 2604.

250°. Lithium [^{36}Cl]chloride was prepared by neutralisation of H^{36}Cl with lithium hydroxide in aqueous methanol.

Kinetics.—The reaction was followed by titration of the acid produced. Aliquot parts (5 c.c.) were titrated in acetone with lacmoid as indicator. For runs in which azide ion was present phenolphthalein was used as indicator and 95% ethanol as titration solvent.

Integrated first-order rate constants k_1, were calculated from the equation: $k_1 = (2{\cdot}3/t) \log a/(a - x)$, where a is the concentration of t-butyl chloride initially, $a - x$ that at time t,

TABLE 4.

Solvent: methanol–water (80 : 20 v/v); 25°. [Bu^{t}Cl] initially ~0·088M; $(a - x)$ expressed in c.c. of 0·054N-NaOH per 5 c.c. portion. The time zero is arbitrary.

Time (min.)	0	30	60	90	120	180	240
Titre (c.c.)	0·22	0·52	0·85	1·07	1·35	1·92	2·35
10^5k_1 (sec.$^{-1}$)	—	2·08	2·23	2·04	2·08	2·16	2·10
Time (min.)	300	360	420	480	541	575	∞
Titre (c.c.)	2·85	3·25	3·62	3·98	4·27	4·40	8·36
10^5k_1 (sec.$^{-1}$)	2·16	2·15	2·10	2·10	2·12	2·08	—

Mean $10^5k_1 = 2{\cdot}12 \pm 0{\cdot}05$ (sec.$^{-1}$).

and t is in seconds. From the results of runs at 25·0° and 35·0° we can calculate approximate values of the Arrhenius parameters: in methanol–water (80 : 20 v/v), $E = 23$ kcal. mole^{-1}; $A = 10^{12}$ sec.$^{-1}$; in methanol–water (75 : 25 v/v), $E = 23$ kcal. mole^{-1}; $A = 2 \times 10^{12}$ sec.$^{-1}$. These values are similar to those found for solvolyses of t-butyl chloride in other solvents. Details of a typical run are in Table 4.

Estimation of Olefin.—Aliquot portions of t-butyl chloride in alkaline aqueous methanol were sealed in tubes. After a convenient time, two tubes were removed. In one, the extent of reaction was determined by acid–base titration; the other was broken under acidic methanol at 0°, an excess of standard bromine in methanol added, the flask swirled, potassium iodide added and the iodine titrated with thiosulphate. Control tests were made on samples taken at the beginning of reaction.

[Bu^{t}Cl] = 0·085M; [NaOH] = 0·10—0·13M. Methanol–water (80 : 20 (v/v).

	25·0°	35·0°
Elimination/Total reaction (moles %)	13·7; 13·1 *	15·3

* Methanol–water 75 : 25 (v/v).

The percentage of olefin elimination is similar to those found for other $E1$ eliminations from t-butyl compounds.[13]

Azide Intervention.—The extent of this was determined at complete reaction, by estimation of acid. The change of azide-ion concentration during reaction was small.

Isotopic Exchange.—A solution of Na^{36}Cl (or Li^{36}Cl) was prepared in aqueous methanol, and the specific activity of a portion determined by using a halogen-quenched liquid counter tube and an Ekco scaler. To the rest, t-butyl chloride was added (at thermostat temperature). After *ca.* one half-life, half the solution was removed and cooled to 0°, and part evaporated under the vacuum of a rotary oil pump. Dry air was passed in to prevent bumping, and the distillate passed through a ½ l. round-bottomed flask. The distillate was trapped in two traps, in series, cooled to −80°. The contents of the traps were treated with sodium hydroxide to hydrolyse the t-butyl chloride. The amount of chloride was determined by potentiometric titration with N/100-silver nitrate. The specific activity was then determined. This procedure was repeated with the residue of the reaction solution after *ca.* 2 half-lives.

It was necessary to make various tests on this method of separation. All experiments were made with alkali in excess over the t-butyl chloride, therefore there was no risk of hydrogen chloride distilling over. (*a*) A portion of the distillate was redistilled under reduced pressure; the specific activity of this redistilled portion was very close (within experimental error) to that of the original distillate. (*b*) Control experiments on the distillation were made (i) with unlabelled t-butyl chloride and sodium chloride and (ii) with radioactive sodium chloride and t-butyl alcohol. The distillates had no perceptible radioactivity.

[13] Ref. 6, p. 442.

TABLE 5.

[Bu^{t}Cl] = 0·085M; [NaOH] = 0·115M; [NaCl] = 0·50M; (A) Solution of Na^{36}Cl used. (B) Distillate pumped off after 50% reaction. (C) Solution (B) after redistillation. (D) Distillate pumped off after 75% reaction. (E) Solution (D) after redistillation.

[NaCl] (mM)	Background			Solution			Specific activity counts (min.$^{-1}$ mmole^{-1} l.)
	Time	Counts	Counts/min.	Time	Counts	Counts/min.	
(A) 4·9	15	165	11	25	25,323	1013	207
	20	220		50	50,640		
(B) 2·87	12	141	11·7	15	711	47·6	12·2
	24	283		28	1335		
				30	1432		
(C) 1·73	7	84	12	18	605	32·7	12·0
	12	145		40	1309		
				42	1360		
(D) 2·18	16	191	11·9	28	1864	66·8	25·2
	20	230		30	2014		
	22	270					
(E) 0·878	30	345	11·9	31	1019	32·4	23·4
	45	554		15	470		

(The differences between counts are within the coincidence error.)

The relative values of the first-order constants for exchange, k_E, and chemical reaction, k_C, were calculated from the equation

$$k_E/k_C = \log\{100/(100 - \%\ \text{exchange})\}/\log\{a/(a - x)\}$$

The change in chloride-ion concentration during the run was ignored; this causes little error for samples taken at 1 half-life. Table 5 contains details of an exchange experiment in methanol–water 75 : 25 (v/v) at 35·0°.

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778. *Anionic Polymerisation of Vinyl Monomers with Butyl-lithium.*

By MAX FRANKEL, ARIEL OTTOLENGHI, MICHAEL ALBECK, and ALBERT ZILKHA.

The anionic polymerisation of various vinyl monomers by use of butyl-lithium was investigated. The effects of concentration of catalyst, temperature, and solvents were studied.

THE polymerisation of isoprene by butyl-lithium has recently been extensively studied.[1] In heterogeneous systems under certain conditions stereospecific polymerisation occurs giving polymers of regular structure, *e.g.*, *cis*-1,4-polyisoprene. We have now studied the polymerisation of methyl methacrylate, acrylonitrile, styrene, and other vinyl monomers using n-butyl-lithium as catalyst. All these monomers have electronegative substituents and are susceptible to anionic polymerisation.

Polymerisation of Methyl Methacrylate.—This was investigated in light petroleum, a non-polar solvent of low dielectric constant, which is a good solvent for the monomer even at low temperature. The polymer, being insoluble, was precipitated on formation.

The dependence of yield of the poly(methyl methacrylate) on the amount of catalyst was investigated. Experiments were carried out (Table 1) with identical quantities and concentrations of methyl methacrylate in light petroleum at −15°. Butyl-lithium, in the

[1] Hsieh and Tobolsky, *J. Polymer Sci.*, 1957, **25**, 245; Morita and Tobolsky, *J. Amer. Chem. Soc.*, 1957, **79**, 5853.

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same solvent, was added in one portion with mechanical stirring; the polymerisation time was 1 hr. throughout. A threshold concentration of catalyst was needed to start the polymerisation, but there was no induction period. The yield increased with increasing amount of catalyst to approximately quantitative values. The molecular weights obtained were high (about 130,000) and did not depend on the amount of catalyst (Table 1). Somewhat lower yields were obtained on adding the monomer dropwise to the catalyst during

TABLE 1. *Polymerisation of methyl methacrylate. Dependence of polymerisation yield on amount of catalyst.*

Experimental Conditions.—Butyl-lithium dissolved in light petroleum (15 ml.) was added in one portion to cooled methyl methacrylate (25 ml.; 2·34 moles/l.) in light petroleum (60 ml.). Polymerisation temperature −15°, time 1 hr.

Catalyst (mmole)	2	3	4	4·5	6	8	10	12	15
[Catalyst] (M)	0·02	0·03	0·04	0·045	0·06	0·08	0·1	0·12	0·15
Polymer (g.)	Trace	Trace	2·5	8·5	17 [a]	18	21 [b,c]	22 [d]	22
Yield (%)	—	—	11	36	73	77	90	94	94
[η] (dl./g.)	—	—	—	—	0·29	0·29	—	—	0·27
$10^{-3}M$ [e]	—	—	—	—	128	128	—	—	116

[e] Average molecular weights of the polymers were calculated from intrinsic viscosities, measured in toluene at 30°, by use of the equation $[\eta] = 6{\cdot}87 \times 10^{-5}M^{0{\cdot}71}$ (Riddle, " Monomeric Acrylic Esters," Reinhold, New York, 1954, p. 64).

[a] Monomer added during 15 min. under otherwise constant conditions gave 12 g. (52%) of polymer. [b] Monomer added during 15 min. under otherwise constant conditions gave 17 g. (73%) of polymer. [c] Catalyst dissolved in 25 ml. of light petroleum, added during 15 min. to monomer in light petroleum (50 ml.) under otherwise constant conditions gave 17 g. (73%) of polymer. [d] Catalyst in light petroleum (15 ml.) added to monomer in benzene under the above conditions, gave 4 g. (17%) of polymer, obtained on evaporation of solvent. Similar yields were obtained with tetrahydrofuran or ether.

15 min. under otherwise constant conditions, so that a small initial concentration of monomer existed (Table 1). Yields did not change either on extending the time of addition from 15 min. to 60 min. or on addition of catalyst to monomer during 15 min.

The progress of the polymerisation, followed under otherwise constant conditions (Table 2), was fast at first; in 10 min. about half the yield was obtained. In the last 30 min. the polymerisation was slow and the yield increased by only 10%.

The effect of temperature was investigated between −30° and +50° (Table 3); increase in temperature lowers the yield. Thus, polymerisation at 50° gave only about 25% of

TABLE 2. *Polymerisation of methyl methacrylate. Dependence of yield on polymerisation time.*

Experimental Conditions.—As in Table 1, except that butyl-lithium (6×10^{-3} mole; 0·06 mole/l.) was used throughout and polymerisation carried out for the time stated.

Time (min.)	5	10	15	20	30	60
Polymer (g.)	3	8 [a]	11	14	15·5	17
Yield (%)	13	34	47	60	67	73

[a] This polymer gave an intrinsic viscosity of 0·25 dl./g. corresponding to $M = 104{,}000$.

the yield of that at −15°. The increase in yield at low temperature may be due to the enhanced stability of the carbanionic propagation centres. The polymers obtained at lower temperature had higher molecular weights (Table 3).

TABLE 3. *Polymerisation of methyl methacrylate. Dependence of yield on polymerisation temperature.*

Experimental Conditions.—As in Table 1, except that butyl-lithium (8×10^{-3} mole; 0·08 mole/l.) was used throughout and the polymerisation carried out at different temperatures.

Temperature [a]	−30°	−15°	30°	50°
Polymer (g.)	18	18 [b]	12·5 [c]	3·5
Yield (%)	77	77	54	15

[a] A smaller amount of catalyst being used (6×10^{-3} mole; concn. 0·06 mole/l.), the polymerisation was more affected by increase in temperature. Thus polymerisation at 10° gave 10 g. of polymer compared with 17 g. at −15°. [b] $[\eta] = 0{\cdot}29$ dl./g.; $M = 128{,}000$. [c] $[\eta] = 0{\cdot}2$ dl./g.; $M = 76{,}000$.

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Preliminary polymerisations in ether, benzene, or tetrahydrofuran (Table 1), *i.e.*, solvents in which the polymer was soluble, gave very low yields even at high concentrations of catalyst.

X-Ray diffaction diagrams of two samples of poly(methyl methacrylate) [one prepared with 0·004 mole of butyl-lithium at −15° (Table 1) and the other with 0·008 mole of butyl-lithium at −50°], pressed in a Carver press at 120°/2000 lb./in.$^{-2}$ and swelled in ether, showed partial crystallinity. Three broad reflection bands appeared having *d*-values of 6·0 ± 0·4 Å (very strong), 2·85 ± 0·15 Å (medium), and 2·5 ± 0·15 Å (weak). The strong reflection

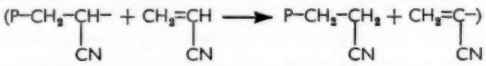
TABLE 4. *Polymerisation of acrylonitrile. Dependence of polymerisation yield on amount of catalyst.*

Experimental Conditions.—Butyl-lithium dissolved in light petroleum (15 ml.) was added in one portion to cooled acrylonitrile (25 ml.; 3·77 mole/l.) in light petroleum (60 ml.). Polymerisation temperature −15°, time 1 hr.

Catalyst (mmole)	1	1·5	2	2·5	3	4	6	10	12
[Catalyst] (mole/l.)	0·01	0·015	0·02	0·025	0·03	0·04	0·06	0·1	0·12
Polymer (g.)	2	2·5	3·5	5	6 [a]	9 [d]	15	16 [e]	18 [b,e]
Yield (%)	10	13	18	25	30	45	75	80	90
[η] (dl./g.)	0·44	—	—	—	—	0·4	—	—	0·37
$10^{-3}M$ *	23·5	—	—	—	—	21	—	—	18·5

* Average molecular weights of the polymers were calculated from intrinsic viscosities measured in dimethylformamide at 30° by use of the equation $[\eta] = 2{\cdot}33 \times 10^{-4}M^{0.75}$ (Cleland and Stockmayer, *J. Polymer Sci.*, 1955, **17**, 473).

[a] Monomer added during 15 min. under otherwise constant conditions gave 2 g. of polymer. [b] Monomer added during 15 min. under otherwise constant conditions gave 15·5 g. (78%) of polymer; [η] = 0·36 dl./g.; M = 18,000. In this case there was a smaller concentration of monomer in the beginning of the polymerisation; nevertheless the molecular weight of the polymer was the same, showing that the degree of polymerisation was independent of the concentration of the monomer and that the termination reaction is dominated by chain transfer with monomer (ref. 3, p. 223):



[c] Ether being used as solvent instead of light petroleum, the yield was 7 g. (35%) of polymer; [η] = 0·11 dl./g.; M = 3750. [d] Catalyst dissolved in light petroleum (15 ml.) was added to monomer in tetrahydrofuran (60 ml.) gave 3 g. of polymer; [η] = 0·18 dl./g.; M = 7000. [e] Catalyst dissolved in light petroleum (15 ml.) was added to monomer in tetrahydrofuran (60 ml.) gave 7 g. (35%) polymer; [η] = 0·14 dl./g.; M = 5000.

can be indexed as an *hkl* reflection (020) on the basis of the unit cell suggested for syndiotactic poly(methyl methacrylate).[2]

Polymerisation of Acrylonitrile.—The dependence of yield of the polyacrylonitrile on the amount of catalyst was investigated. Comparable experiments were carried out (Table 4) in light petroleum at a constant temperature of −15°. The catalyst, in the same solvent, was added in one portion and the polymerisation was carried on for 1 hr. The acrylonitrile is only slightly soluble in light petroleum at −15° and so two liquid phases were formed during the polymerisation. A threshold concentration of catalyst was needed to start the polymerisation but this was less than in the case of methyl methacrylate. This might be due to the presence of the nitrile group which is much more electronegative than the ester group. The molecular weights of the polymers were generally much lower than those of poly(methyl methacrylate). The reactive α-hydrogen atom of the acrylonitrile can enter into chain transfer reactions which lower the molecular weight. Molecular weight did not depend on the amount of catalyst. Other polymerisation experiments carried out by addition of monomer to catalyst during 15 min. (Table 4) under otherwise constant conditions gave somewhat lower yields especially with small amounts of catalyst.

Temperature had a pronounced effect on polymerisation (Table 5). Thus a polymerisation at 10° gave less than 50% of the yield of a similar one at −15°. The molecular weights of the polymers obtained at lower temperature were much higher owing to the

[2] Stroupe and Hughes, *J. Amer. Chem. Soc.*, 1958, **80**, 2341.

TABLE 5. *Polymerisation of acrylonitrile. Dependence of yield on polymerisation temperature.*

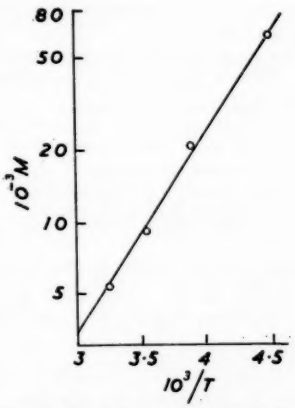
Experimental Conditions.—As in Table 4, except that butyl-lithium (4×10^{-3} mole; 0·04 mole/l.) was used and the polymerisation carried out at different temperatures.

Temperature	−50°	−15°	10°	35°
Polymer (g.)	6	9	4	2·5
Yield (%)	30	45	20	13
$[\eta]$ (dl./g.)	0·94	0·4	0·22	0·15
$10^{-3}M$	64	21	9·25	5·5

decreased effect of chain transfer. A semi-logarithmic plot (Figure) of molecular weight against the reciprocal of the polymerisation temperature for acrylonitrile gave a straight line, whose slope [3] corresponds to a difference in activation energy between propagation and termination of 4 kcal./mole.

Polymerisations in tetrahydrofuran or ether instead of light petroleum gave lower yields and the polymers had lower molecular weights (Table 4).

X-Ray diffraction diagram of a sample of polyacrylonitrile prepared at −50° (Table 5) showed two broad reflections having *d*-values of 5·55 ± 0·4 Å (strong), 3·4 ± 0·3 Å (medium). The spacing of 5·3 Å is associated with the distance between chains through the hydrogen-bonded nitrile groups.[4] The second reflection is absent from ordinary undrawn polyacrylonitrile preparations.



Molecular weight of polyacrylonitrile as a function of temperature.

Polymerisation of Styrene.—The anionic polymerisation of styrene with butyl-lithium was markedly different from those of methyl methacrylate or acrylonitrile. The same experimental conditions being used as for the latter monomers [catalyst (0·01 mole) added to styrene (1 vol.) in light petroleum (3 vol.) at −15°], a light brown colour appeared owing to the formation of styryl carbanions, but no significant polymerisation had occurred after 1 hr. Carbonation of the product with solid carbon dioxide showed that most of the butyl-lithium remained unchanged and was converted into valeric acid. Doubling the amount of catalyst (0·02 mole) did not induce significant polymerisation (Table 6, *A*). In other experiments styrene was added dropwise during 15 min. to the catalyst dissolved in light petroleum (3 vol.) at −15° so that a great initial concentration of catalyst existed; here also only slight polymerisation occurred. A higher temperature increased the polymerisation considerably, and when the temperature was increased to 50° the styrene polymerised completely to a heavy red oil which solidified under light petroleum. These experiments show that the styrene, having a weak electronegative group (phenyl) needs a high activation energy for initiation of the polymerisation, unlike the previous monomers. No activation energy is necessary for propagation [5] as this involves the approach of an ion to a neutral molecule in light petroleum which has a low dielectric constant.

In both ether and tetrahydrofuran styrene polymerised at −15°. This may be due to solvation of the catalyst (the lithium cation yielding the green complex with the tetrahydrofuran owing to the formation of an electron octet by means of co-ordination valencies with the oxygen atom [6]). This apparently lowers the activation energy of the initiation.

On the other hand it was possible to polymerise pure styrene even with very small

[3] Flory, "Principles of Polymer Chemistry," Cornell Univ. Press, New York, 1953, p. 218.
[4] Schildknecht, "Vinyl Polymers," Wiley, New York, 1952, p. 276.
[5] Billmeyer, "Polymer Chemistry," Interscience, New York, 1957, p. 267.
[6] Uelzmann, *J. Polymer Sci.*, 1958, **32**, 457.

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TABLE 6. *Polymerisation of styrene.*

A. Experimental Conditions.—Polymerisations were carried out in a three-necked flask with 25 ml. of styrene (0·218 mole) under the conditions indicated below; polymerisation time, 1 hr.

Solvent for monomer (ml.)	Solvent for catalyst (ml.)	[Styrene] (M)	Butyl-lithium (mmole)	[Butyl-lithium] (M)	Temp.	Polymer (g.)	Yield (%)
Pet (60)	Pet (15)	2·18	10	0·1	−15°	Trace [a,b]	
Pet (50)	Pet (25)	2·18	20	0·2	−15	Trace [c]	
Pet (60)	Pet (15)	2·18	10	0·1	0	4	(18%) [d]
Pet (25)	Pet (50)	2·18	12	0·12	40	22	(97%) [e]
Pet (25)	Pet (30)	2·73	10	0·15	50	22	(97%) [f,g]
Ether (50)	Pet (35)	1·98	20	0·182	−15	19	(84%) [e,i]
Ether (50)	Pet (15)	2·42	11	0·122	0	21	(93%) [e,h]
None	Ether (10)		10		−10	22	(97%) [j]
Tet (60)	Pet (15)	2·18	5	0·05	−15	10	(44%) [k]
Tet (60)	Pet (15)	2·18	10	0·1	−15	22	(97%) [e]

Pet = light petroleum. Tet = tetrahydrofuran.

[a] Trace indicates the formation of 1 g. of polymer or less. [b] Catalyst added to monomer in one portion. [c] Cooled catalyst added during 3 min. [d] $[\eta] = 0{\cdot}049$ dl./g.; $M = 2300$. Molecular weights were calculated according to the equation of Waack *et al.* (Ref. 9). $[\eta] = 1{\cdot}6 \times 10^{-4}M^{0{\cdot}74}$. [e] Monomer added to catalyst during 30 min. [f] Catalyst added to monomer at −10°, then reaction mixture was heated to 50°. [g] $[\eta] = 0{\cdot}048$ dl./g.; $M = 2200$. This is in good agreement with the molecular weight calculated from the formula:

$$\frac{\text{Moles of styrene} \times \text{Molecular weight of styrene}}{\text{Moles of catalyst}} = \frac{0{\cdot}218 \times 104}{0{\cdot}01} = 2265$$

[h] $[\eta] = 0{\cdot}043$ dl./g.; $M = 1900$. [i] $[\eta] = 0{\cdot}031$ dl./g.; $M = 1200$. [j] Styrene was added slowly to catalyst to prevent uncontrollable polymerisation.

B. Experimental Conditions.—Polymerisations carried out at room temperature in a 500 ml. wide-mouthed bottle. The butyl-lithium was added in one portion from a pipette to undiluted styrene (20 ml.); catalyst was added until sudden polymerisation of the styrene occurred.

Catalyst (mmole)	2	6	7·6
Solvent for catalyst (ml.)	Ether (3)	Ether (9)	Pet (6)
Time of addition (sec.)	4	10	8
Polymer (g. and % yield)	14 (77%)	16 (88%)	16 (88%)

amounts of catalyst if this was added within a few seconds as a concentrated solution (Table 6, *B*). The heat generated locally will greatly further the initiation step and cause very rapid polymerisation of the monomer. In these reactions, the styrene " flash "-polymerised completely and the temperature soared to 110°, indicating the strong exothermic polymerisation. Addition of the catalyst during a comparatively larger time interval enables the reaction heat to dissipate and more catalyst is needed for complete polymerisation. In these " flash "-polymerisations the polymerising styrene expanded to a large volume and yielded a friable mass reminiscent of foam polymerisation products, the low-boiling solvents (ether or light petroleum) serving as the blowing agents.

An important feature of the polymerisation of styrene is that the polymer obtained is dull red owing to the presence of carbanion end-groups, showing that no termination step has occurred and thus " living polymers " [7] are obtained. These are similar to the living polymers prepared by Szwarc, Levy, and Milkovich by electron-transfer catalysts in non-proton donating solvents.[7] The polymers, possessing still intact carbanion propagation centres, polymerise other freshly added monomers such as styrene, methyl methacrylate, or acrylonitrile and thus produce block polymers (see Experimental). On being exposed to air, or on addition of alcohol or water, the colour disappeared completely as the carbanions were destroyed. These polymers reacted with Michler's ketone in benzene under the conditions of the Gilman and Schultze's test [8] for organometallic compounds; however the characteristic green colour developed only after several hours' standing, unlike those given by simple organometallic compounds such as butyl-lithium. From the benzene solution it was possible to precipitate a green polystyrene with methanol.

[7] Szwarc, Levy, and Milkovich, *J. Amer. Chem. Soc.*, 1956, **78**, 2656.

[8] Gilman and Schultze, *J. Amer. Chem. Soc.*, 1925, **47**, 2002; Vogel, " Practical Organic Chemistry," 3rd edn., Longmans, Green & Co., London, 1956, p. 241.

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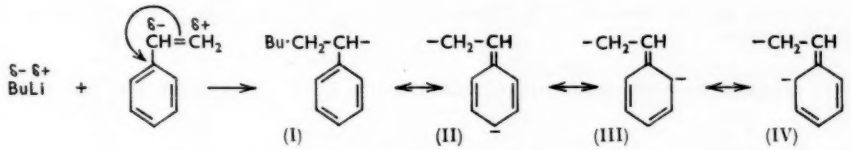
A characteristic of " living " polymers is that the molecular weight [9] depends only on the ratio of the monomer to the catalyst, more catalyst proportionately decreasing the molecular weight, and is independent of temperature. The " living " polymers (Table 6, *A*) show such behaviour. Block copolymers can be produced, having polystyrene of the required molecular weight, by varying the quantity of the catalyst and carrying the polymerisation of the styrene to completion before adding other monomers.

The absence of the termination step from the polymerisation of styrene by butyl-lithium is plausible for the following reasons: (*a*) The polymerisations were carried out in non-proton donating solvents such as light petroleum, so that no termination will occur by abstraction of a proton from the solvent. (b) The styryl carbanions are resonance-stabilised by the benzene ring and four resonance structures are possible (I—IV).



Polymerisation of Other Monomers.—Some experiments on the polymerisation of methyl acrylate, butyl acrylate, allyl acetate, vinyl acetate, and dimethyl maleate with butyl-lithium were carried out. In all cases, variation of the amounts of catalyst and polymerisation temperatures gave only viscous or semi-solid polymers in low yields.

Experimental

Materials.—Light petroleum (b. p. 60—80°), ether, tetrahydrofuran, and benzene were dried (Na), and boiled under nitrogen before use. Methyl methacrylate, acrylonitrile, methyl acrylate, and vinyl acetate were dried and distilled under nitrogen. Styrene was distilled over sulphur. Nitrogen was freed from oxygen by passage through a quartz tube containing fresh copper wire at 600°, then through a 5% alkaline permanganate solution followed by a solution of 20% pyrogallol in 20% sodium hydroxide, and dried (conc. H_2SO_4). n-Butyl-lithium, prepared as before,[10] was kept in an ice-box and its concentration in the solvent checked by titration before use.

Polymerisation of Monomers.—The addition of reagents and the polymerisations were carried out under nitrogen. Into a three-necked flask fitted with a high-speed stirrer, dropping funnel, and a gas-adapter for introducing nitrogen, the required amounts of monomer and solvent were added. The flask was cooled to the required temperature and kept thereat. The catalyst solution was then added. The polymerisation was stopped after the required time by adding 50 ml. of cooled hydrochloric acid (10%). The polymer was filtered off, washed with water, light petroleum, and methanol to remove monomer, and then dried to constant weight in a vacuum-desiccator at room temperature or in an electric oven at 60°.

" Flash "-polymerisation of styrene, in which the catalyst solution was added during several seconds to the undiluted monomer, was carried out in wide-mouthed Pyrex bottles and the catalyst added from a pipette.

Viscosities of polymer solutions were measured in an Ostwald or an Ostwald–Fenske viscosimeter.

Preparation of a Block Polymer of Styrene–Acrylonitrile.—" Living " polymer of styrene was prepared by the rapid addition of a concentrated solution of butyl-lithium in ether. The polymer, obtained as a dull red mass, gave a negative Gilman–Schultze test for organometallic compounds, indicating absence of residual butyl-lithium.

0·3 g. of this polymer was added to 4 ml. of distilled acrylonitrile in a test-tube flushed with nitrogen. Polymerisation started immediately with evolution of heat, and the polystyrene particles became covered with brown-red polyacrylonitrile. After 2 hr. the polymer was filtered off, washed with light petroleum, then with water to remove lithium salts, and dried

[9] Waack, Rembaum, Coombes, and Szwarc, *J. Amer. Chem. Soc.*, 1957, **79**, 2026.
[10] Frankel, Rabani, and Zilkha, *J. Polymer Sci.*, 1958, **28**, 387.

in vacuo. The polymer was purified by boiling it in benzene. This removed all the polystyrene and block polymers low in acrylonitrile, leaving 0·35 g. of insoluble polymer. When this was boiled with acetone, 0·09 g. of a reddish-brown insoluble polymer remained. Evaporation of the acetone *in vacuo* gave 0·23 g. of block polymer, analysis of which gave 16·6% of nitrogen, showing it to consist of 63% of acrylonitrile and 37% of styrene. It was insoluble in chloroform or dioxan, and melted at *ca.* 190—200° (decomp.).

The polymer insoluble in acetone gave on analysis 21% of nitrogen, showing it to consist of 80% of acrylonitrile and 20% of styrene. It decomposed at *ca.* 220—230°. This block polymer might be contaminated with free polyacrylonitrile, if any such polymer was formed during the polymerisation by chain transfer.

Infrared spectra of the block polymer showed absorption at 4·45 μ (cyanide group of the polyacrylonitrile) and at 6·2 μ, 6·65 μ, and 13·4 μ (aromatic ring of polystyrene).

We thank Mr. Zvi Kalman of the Physics Department of this University for carrying out the *X*-ray work.

Department of Organic Chemistry,
Hebrew University, Jerusalem, Israel. [*Received, May 12th*, 1959.]

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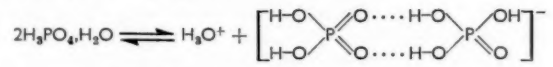
779. *Anomalous Conduction in Phosphoric Acid Hemihydrate,* $2H_3PO_4,H_2O$.

By N. N. Greenwood and A. Thompson.

Transport measurements have established that the high conductivity of fused phosphoric acid hemihydrate is due to a proton-switch mechanism similar to that observed in water, sulphuric acid, and orthophosphoric acid. The conductivity, viscosity, and density have been measured between 25° and 70°, and the variation of activation energies with temperature determined. If the proton-switch mobility of the anomalously conducting ions is similar to that in water and sulphuric acid, then the hemihydrate is about 4·5% dissociated into ions, corresponding to an autoprotolysis constant $K_{ap} \simeq 4{\cdot}4 \times 10^{-2}$ mole^2 kg.$^{-2}$ (cf. $K_{ap} \simeq 1{\cdot}7 \times 10^{-2}$ for anhydrous orthophosphoric acid). The proposed ionization is



The reduction in conductivity which occurs when potassium salts are dissolved in the hemihydrate is ascribed to the removal of solvent molecules from the conduction chain by solvation of the added cations.

Addition of water to anhydrous phosphoric acid increases its conductivity and decreases its viscosity. No discontinuity in conductivity is observed[1] at the composition $2H_3PO_4,H_2O$ although the hemihydrate has long been recognised as a distinct solid phase.[2] The conductivity of the fused hemihydrate is nearly twice that of the anhydrous acid and this, coupled with the fact that addition of water to the system increases the concentration of the anomalously conducting dihydrogen phosphate ion, suggests that the hemihydrate, like the parent acid, conducts by a proton-switch mechanism. This has now been verified by transport measurements on solutions of potassium dihydrogen phosphate in the fused hemihydrate. In addition, the physical properties of the compound have been studied systematically over a range of temperature and compared with the isolated data in the literature.

The experimental methods have been described previously.[1]

[1] Greenwood and Thompson, *J.*, 1959, 3485.
[2] Joly, *Bull. Soc. chim. France*, 1886, **45**, 329.

Results

Phosphoric acid hemihydrate, prepared by repeated fractional crystallization of " AnalaR " phosphoric acid of appropriate composition, had m. p. 29·30° ± 0·02°. Early literature values are 29·35°,[3] 29·32°,[4] and 29·25° [5] and a recent careful redetermination [6] also gave 29·25°.

The densities (Table 1) can be fitted by the equation $d_4^t = 1{\cdot}7747 - 7{\cdot}80 \times 10^{-4}t$. No determinations referring specifically to the hemihydrate have been published but interpolation of Ross and Jones's [4] results gives values (compared with ours in parentheses) of 1·7611 (1·7550) at 25°, 1·750 (1·7433) at 40°, and 1·735 (1·7279) at 60°. Extrapolation of the data of Knowlton and Mounce [7] to the composition of the hemihydrate gives a value at 25° of 1·7657. The molar volume at 25° is 122·0 ml. which is 1·0 ml. less than the sum of the molar volumes of the components, *i.e.*, the apparent volume occupied by one mole of water when added to two moles of phosphoric acid is 17 rather than 18 ml.

Table 1. *Density, viscosity, and conductivity of* $2H_3PO_4,H_2O$.

Temp.	d_4^t (g. cm.$^{-3}$)	η (cP)	$10^2\kappa$ (ohm^{-1} cm.$^{-1}$)	μ (ohm^{-1} cm.^{2} mole^{-1})	$\mu\eta$ (ohm^{-1} cm.^{2} cP mole^{-1})
25°	1·7548	70·64	7·008	8·565	604·9
30	1·7506	55·60	8·230	9·840	547·0
35	1·7471	46·73	9·592	11·75	545·0
40	1·7433	39·76	10·99	13·49	536·0
45	1·7396	32·46	12·54	15·44	501·0
50	1·7357	27·57	14·16	17·46	492·5
55	1·7318	23·64	15·85	19·58	463·0
60	1·7279	20·54	17·50	22·20	445·6
65	1·7240	17·87	19·26	23·11	427·4
70	1·7201	15·65	21·21	26·39	414·0

The viscosity of phosphoric acid hemihydrate has not previously been reported. At 25° its value is only 40% of the viscosity of the parent acid but is still 79 times greater than that of water. Values in Table 1 can be fitted by an expression of the type $\eta = \eta_0 \exp(C_\eta/\boldsymbol{R}T^2)$ as shown by the linear plot in the Figure. This implies [8] that the activation energy of viscous flow is inversely proportional to the temperature in the range studied, the decrease at higher temperatures being related to the decreasing extent of hydrogen bonding. Representative values of the activation energy are presented in Table 2.

Table 2. *Activation energies for phosphoric acid hemihydrate.*

Temp.	E_κ (kcal. mole^{-1})	E_μ (kcal. mole^{-1})	E_η (kcal. mole^{-1})
25°	5·38	5·52	7·07
40	5·13	5·44	6·95
60	4·81	4·94	6·33

The electrical conductivity of phosphoric acid hemihydrate, unlike that of phosphoric acid itself, showed no variation with time and was accurately reproducible in two different cells and on different samples provided these were fractionally crystallized in a closed system attached directly to the conductivity cell. The values found lie between the two published figures for the conductivity; [5,9] these refer to 29·3° and are $8{\cdot}26 \times 10^{-2}$ and $7{\cdot}938 \times 10^{-2}$ compared with the present value of $8{\cdot}051 \times 10^{-2}$ ohm^{-1} cm.$^{-1}$. At 35° Rabinowitsch [5] found a value of $9{\cdot}63 \times 10^{-2}$ compared with the present $9{\cdot}592 \times 10^{-2}$ ohm^{-1} cm.$^{-1}$. The Figure shows that the data in Table 1 conform to the relation $\kappa = \kappa_0 \exp(-C_\kappa/\boldsymbol{R}T^2)$ and values of the activation energies at three temperatures are given in Table 2.

The conductivity of the solid is much lower than that of the fused compound and, near the m. p., it tended to drift for some time before equilibrium values were obtained. The results

[3] Smith and Menzies, *J. Amer. Chem. Soc.*, 1909, **31**, 1183.
[4] Ross and Jones, *ibid.*, 1925, **47**, 2165.
[5] Rabinowitsch, *Z. anorg. Chem.*, 1923, **129**, 60.
[6] Egan and Wakefield, *J. Phys. Chem.*, 1957, **61**, 1500.
[7] Knowlton and Mounce, *Ind. Eng. Chem.*, 1921, **13**, 1157.
[8] Greenwood and Thompson, *J.*, 1959, 3474.
[9] Smith and Menzies, *J. Amer. Chem. Soc.*, 1909, **31**, 1191.

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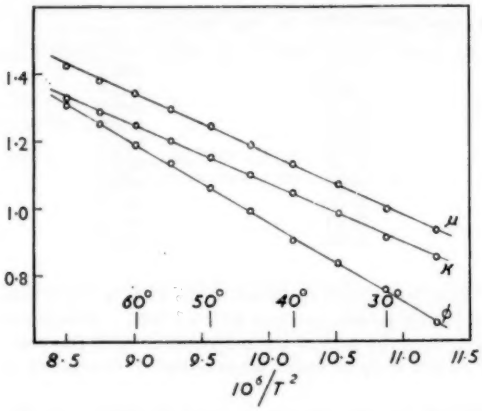
confirm the premelting increase in conductivity implied by Rabinowitsch's work [5] and typical values of $10^3\kappa$ ohm^{-1} cm.$^{-1}$ (at $t°$) are 0·97 (19°), 1·22 (21°), 1·63 (23°), 2·36 (25°), and 3·12 (26°). At 25°, *i.e.*, 4·3° below the m. p., the conductivity of the solid was 30 times smaller than that of the supercooled liquid.

Electrolysis of the fused hemihydrate gave hydrogen at the cathode and oxygen at the anode as expected. Transport measurements on solutions of potassium dihydrogen phosphate in the hemihydrate were made by the method previously described.[1] No migration of potassium ions was detected, the entire current being carried by a switch mechanism involving the di-



Conductivity and fluidity of $2H_3PO_4,H_2O$. The vertical scale represents values of (2 + log κ), log μ, and (0·5 + log ϕ).

hydrogen phosphate ion. For example, the passage of 740 coulombs (41 mA for 5 hr.) through a $2·66 \times 10^{-2}$ molar solution of potassium dihydrogen phosphate did not change the potassium ion concentration in any of the three compartments of the transport cell.

Discussion

The transport measurements establish unambiguously that the dihydrogen phosphate ion has an anomalous mobility in the hemihydrate, as it has in the anhydrous acid, but the extent of self-ionization of the solvent cannot be determined without some knowledge of the absolute value of this mobility. It has been argued [1] that a value of 20×10^{-4} cm.^{2} sec.$^{-1}$ volt^{-1} should be reasonably close to the actual mobility. Substitution of this and the value of the specific conductivity at 25° into the expression $\kappa = nev$ gives the concentration, n, of dihydrogen phosphate ions as $2·20 \times 10^{20}$ ions per ml. (0·21 molal). As the molar volume of the hemihydrate $2H_3PO_4,H_2O$ is 122·0 ml., 1 ml. contains $4·94 \times 10^{21}$ " molecules " of solvent. Hence the degree of ionic dissociation is 4·5%.

The structure of phosphoric acid hemihydrate has not been determined and, although some incomplete *X*-ray data have been published,[10] no structure for the compound has been suggested. Phosphoric acid itself undergoes ionic dissociation according to eqn. (1).

$$2H_3PO_4 \rightleftharpoons H_4PO_4^+ + H_2PO_4^- \quad \ldots\ldots\ldots\ldots \quad (1)$$

Addition of water to the system removes a proton from the phosphoric acidium cation thus forming a hydroxonium ion and liberating a molecule of phosphoric acid. When an equimolar quantity of water has been added the reaction can be represented as (2), although

$$H_3PO_4 + H_2O \longrightarrow H_3PO_4,H_2O \rightleftharpoons H_3O^+ + H_2PO_4^- \quad \ldots\ldots \quad (2)$$

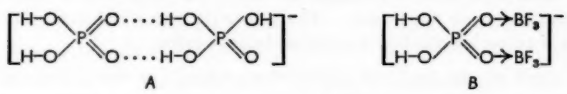
the monohydrate does not exist as a separate solid phase. When only a hemimolar quantity of water has been added, the liberated molecule of phosphoric acid can solvate

[10] Smith, Brown, and Lehr, *J. Amer. Chem. Soc.*, 1955, **77**, 2728.

the dihydrogen phosphate ion as shown in (3), and this is the suggested mode of ionic dissociation of this compound.

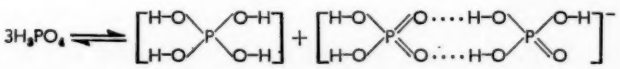
$$2H_3PO_4 + H_2O \longrightarrow 2H_3PO_4,H_2O \rightleftharpoons H_3O^+ + H_3PO_4,H_2PO_4^- \quad . \quad . \quad . \quad . \quad . \quad (3)$$

The stability of the monohydrate thus arises from the ability of the phosphoric acid molecule to form hydrogen bonds to both the phosphoryl oxygen atoms of the dihydrogen phosphate ion, the structure of the anion being shown in *A*. Such a structure would



A B

facilitate proton switches since a proton added to the free phosphoryl oxygen atom could, in effect, be liberated at the other end of the ion. The structure is similar to that postulated for the anion of the boron trifluoride complex of phosphoric acid, *B*, the removal of the hydrogen bridges effectively suppressing the proton-switch conduction mechanism in this compound.[11] It is probable that the dihydrogen phosphate ion is solvated in the anhydrous acid also and that the dissociation equilibrium (1) is more accurately represented by (4). The formation of a hemihydrate rather than a monohydrate in the system is thereby explained.



. . . (4)

On the basis of eqn. (3) as the autoprotolysis equilibrium it can be seen that the formation of each anomalously conducting anion is accompanied by one hydroxonium ion. As the estimated concentration of the anion in the melt at 25° is 0·21 molal, the autoprotolysis constant is $K_{ap}(2H_3PO_4,H_2O) \simeq 4{\cdot}4 \times 10^{-2}$ mole^2 kg.$^{-2}$. This is slightly larger than the value obtained similarly for the parent acid,[1] $K_{ap}(H_3PO_4) \simeq 1{\cdot}7 \times 10^{-2}$ mole^2 kg.$^{-2}$.

The reduction in conductivity which occurs on addition of potassium dihydrogen phosphate to the molten hemihydrate may be due to the removal of phosphoric acid molecules from the conduction chains by solvation of the potassium ions. To test this hypothesis, other potassium salts were investigated in the range 0—0·2 molal. Potassium sulphate and dipotassium hydrogen phosphate both lowered the conductivity of the solvent, these salts being chosen because (*a*) they were anhydrous, (*b*) they contained twice as many potassium ions per ml. as potassium dihydrogen phosphate, and (*c*) their anions were similar in size and shape to the dihydrogen phosphate ion. Potassium perchlorate was insoluble. The rate of decrease of conductivity as a function of molality was the same for both salts and was more than twice as great as for potassium dihydrogen phosphate. The decrease per potassium ion is rather less for this solute because of the compensating effect of simultaneously adding the anomalously conducting dihydrogen phosphate ion. In fact, at concentrations below 0·03 molal there were indications that addition of potassium dihydrogen phosphate to the hemihydrate did not lower the conductivity of the system. There is clearly considerable scope for extensive cryoscopic and ion-transference experiments in this solvent; it can readily be obtained pure, melts at a convenient temperature, and, unlike phosphoric acid itself, has an accurately reproducible m. p. and conductivity, neither of which vary with time due to secondary equilibria.

We thank the University of Nottingham for a Research Scholarship (to A. T.).

THE UNIVERSITY, NOTTINGHAM. [*Received, June 10th,* 1959.]

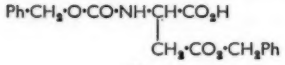
[11] Greenwood and Thompson, *J.*, 1959, 3493.

780. *Amino-acids and Peptides. Part XIV.* Further Studies on the Synthesis of Aspartyl-peptides.*

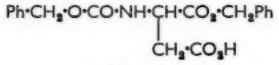
By (Miss) P. M. Bryant, R. H. Moore, (Miss) P. J. Pimlott, and G. T. Young.

α-L-Aspartyl-L-leucine, and α- and β-L-aspartyl-L-aspartic and -L-glutamic acid, have been synthesised through the appropriate monobenzyl ester (I) or (II) of benzyloxycarbonyl-L-aspartic acid. A new route to α-benzyl L-aspartate has been developed. The esters (I) and (II) have been coupled also with ε-benzyloxycarbonyl-L-lysine benzyl ester.

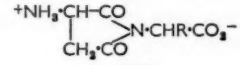
The classical method of synthesis of aspartyl-peptides, by the action of an amino-ester on benzyloxycarbonylaspartic anhydride,[1] yields a mixture of α- and β-aspartyl derivatives,[2] and although in some cases these can be separated,[2,3] in others (*e.g.*, the preparation of the aspartyl-leucines) [4] the separation is unsatisfactory. An alternative route to α-aspartyl-peptides [5] is through β-benzyl benzyloxycarbonyl-L-aspartate (I) prepared by the partial hydrolysis of the dibenzyl ester.[6] We have coupled this intermediate with the appropriate amino-acid benzyl esters for the synthesis of α-L-aspartyl-L-leucine, -L-aspartic acid, and



(I)



(II)



(III)

-L-glutamic acid. In the first case, we used the carbonic mixed anhydride [7] and the ethylene phosphorochloridite ("amide procedure" [8]) methods of coupling, but in the later work we found the use of dicyclohexylcarbodi-imide [9] most satisfactory. The subsequent hydrogenation to remove the benzyloxycarbonyl and the benzyl ester protecting groups was effected without added acid, as evaporation of solutions of the peptides in the presence of mineral acid gave traces of an impurity which is probably the corresponding aspartimide (III) (cf. ref. 10).

The analogous intermediate for the synthesis of β-aspartyl-peptides, α-benzyl benzyloxycarbonyl-L-aspartate (II), is well known,[11] but its preparation from benzyloxycarbonyl-L-aspartic anhydride involves careful purification from its β-isomer. We have developed an alternative preparation, in which α-benzyl L-aspartate is obtained by the controlled cleavage of dibenzyl L-aspartate with hydriodic acid in acetic acid, a reaction similar to that by which α-benzyl L-glutamate can be prepared.[12] Benzyloxycarbonylation gave the required intermediate, from which β-L-aspartyl-L-aspartic acid and -L-glutamic acid were prepared. In each case, dicyclohexylcarbodi-imide was used for the coupling.

By controlled hydrolysis of 3,6-biscarboxymethyl-2,5-dioxopiperazine, Fischer and Koenigs [13] obtained a product which they provisionally formulated as α-aspartylaspartic acid; Greenstein [14] titrated electrometrically a solution of the dipeptide prepared in this

* Part XIII, *J.*, 1959, 2626.

[1] Bergmann and Zervas, *Ber.*, 1932, **65**, 1192.
[2] Le Quesne and G. T. Young, *J.*, 1952, 24.
[3] John and G. T. Young, *J.*, 1954, 2870.
[4] *Idem*, unpublished work.
[5] Miller, Neidle, and Waelsch, *Arch. Biochem. Biophys.*, 1955, **56**, 11.
[6] Berger and Katchalski, *J. Amer. Chem. Soc.*, 1951, **73**, 4084.
[7] Boissonnas, *Helv. Chim. Acta*, 1951, **34**, 874; Vaughan, *J. Amer. Chem. Soc.*, 1951, **73**, 3547; Wieland and Bernard, *Annalen*, 1951, **572**, 190.
[8] R. W. Young, Wood, Joyce, and Anderson, *J. Amer. Chem. Soc.*, 1956, **78**, 2126.
[9] Sheehan and Hess, *ibid.*, 1955, **77**, 1067.
[10] Swallow, Lockhart, and Abraham, *Biochem. J.*, 1958, **70**, 359.
[11] Bergmann, Zervas, and Salzmann, *Ber.*, 1933, **66**, 1288; Miller, Behrens, and du Vigneaud, *J. Biol. Chem.*, 1941, **140**, 411.
[12] Sachs and Brand, *J. Amer. Chem. Soc.*, 1953, **75**, 4610.
[13] Fischer and Koenigs, *Ber.*, 1907, **40**, 2048.
[14] Greenstein, *J. Biol. Chem.*, 1931, **93**, 479.

way and found the expected ionisable groups, but the material was not isolated. α- and β-L-Aspartyl-L-glutamic acid had previously been prepared, with some difficulty, from benzyloxycarbonyl-L-aspartic anhydride, by Le Quesne and Young.[2] Shiba, Yamakita, and Kaneko[15] later reported the synthesis of these dipeptides by a similar route. No specific rotation is quoted for the second-named compound, but for the first they found $[\alpha]_D^{19}$ −3·6°, whereas Le Quesne and Young reported $[\alpha]_D^{25}$ +5·6°, in water. We were therefore glad of the opportunity which the present synthesis, by an entirely different route, gave to redetermine this constant, and we find $[\alpha]_D^{18}$ +6·3°. Since the β-isomer has $[\alpha]_D^{18}$ −10·5° in water, it seems likely that Shiba, Yamakita, and Kaneko's separation of isomers was incomplete. Our dipeptide melted at 145—150°, in comparison with 150—155°[2] and 134—135°,[15] but in our experience melting points are unreliable for the characterisation of peptides.

We record also in this paper the coupling of the esters (I) and (II) with ε-benzyloxycarbonyl-L-lysine benzyl ester. These reactions could not be effected under normal conditions. The use of ethylene phosphorochloridite ("amide" or "standard" procedure[8]) gave little product; the ester (I) was converted into the phenyl thiolester, through the carbonic mixed anhydride,[16] but again condensation with the lysine component was unsuccessful. The *p*-nitrophenyl thiolesters were prepared similarly from (I) and (II), and gave satisfactory yields of coupling products, but it proved difficult to remove all traces of di-*p*-nitrophenyl disulphide, and catalytic hydrogenation failed to remove the benzyloxycarbonyl and the benzyl ester groups completely. Removal of these protecting groups by the action of hydrogen bromide in acetic acid at 60°[17] was accompanied by the formation of a substantial amount of a by-product which moved as a cation during electrophoresis at pH 5·1 and gave a yellow colour with ninhydrin; this may have been the aspartimide {III; R = $[CH_2]_4{\cdot}NH_3^+Br^-$}, analogous to that formed by the action of acid on ε-aspartyl-lysines.[10] Removal of the protecting groups by sodium in liquid ammonia[18] also gave a by-product which behaved similarly on electrophoresis. Finally, successful couplings were effected in moderate yield by using the mixed anhydride with isobutyl hydrogen carbonate under forcing conditions. Hydrogenation of the products gave materials which are clearly α-(α- and β-L-aspartyl)-L-lysine respectively, but we have been unable to recrystallise the small amounts available satisfactorily, and we record here only the protected derivatives.

An unusual side reaction was encountered during the acylation of α-benzyl L-aspartate by benzyl chloroformate, in the presence of aqueous sodium hydrogen carbonate. On two occasions, early in the reaction a considerable amount of a white solid separated, and there was isolated from the product a compound we believe to be α-*O*-benzyl-*N*-benzyloxycarbonyl-β-L-aspartic anhydride. The same material was prepared by the action of cold acetic anhydride on α-benzyl benzyloxycarbonyl-L-aspartate; the infrared absorption differed notably from that of α-benzyl benzyloxycarbonyl-L-aspartate in having a strong peak at 1805 cm.$^{-1}$ (in Nujol paste).*

In earlier papers of this series[2,3] it was noted that the β-aspartyl peptides described there were distinguishable from the α-isomers by the characteristic blue colour given when paper chromatograms were developed with ninhydrin, and this distinction has been confirmed by other workers.[19] The β-aspartyl-peptides reported here give the typical

* From an attempted coupling, by the mixed carbonic anhydride method, of benzyloxycarbonyl-asparagine, Leach and Lindley (*Austral. J. Chem.*, 1954, **7**, 173), isolated a substance which was considered to be the symmetrical anhydride.

[15] Shiba, Yamakita, and Kaneko, *J. Inst. Polytechnics, Osaka City Univ., Ser. C*, 1956, **5**, 144.
[16] Wieland, Schäfer, and Bokelman, *Annalen*, 1951, **573**, 99.
[17] Ben-Ishai and Berger, *J. Org. Chem.*, 1952, **17**, 1564.
[18] Sifferd and du Vigneaud, *J. Biol. Chem.*, 1935, **108**, 753.
[19] Liwschitz and Zilkha, *J. Amer. Chem. Soc.*, 1954, **76**, 3698; 1955, **77**, 1265; Liwschitz, Edlitz-Pfeffermann, and Lapidoth, *ibid.*, 1956, **78**, 3069; Liwschitz and Zilkha, *J.*, 1957, 4394; Zilkha and Liwschitz, *J.*, 1957, 4397.

blue colour; it is, however, important in this test that after spraying with ninhydrin the paper should be dried rapidly at 100—120°; drying at lower temperatures gives various colours, but never, with the β-peptides we have examined, the purple which is obtained from their α-isomers.

Experimental

M. p.s were determined on the Kofler block. Infrared spectra were recorded on a Perkin-Elmer model 21 spectrophotometer. The solvents used for paper chromatography (descending flow) were (*a*) butan-1-ol–water–acetic acid (62 : 26 : 12) and (*b*) phenol–water (80 : 20) in the presence of 0·1% aqueous ammonia. In these solvents, aspartic acid had R_F 0·15 and 0·06, respectively. Electrophoresis (at 7 v/cm.) was carried out in a Durrum type of apparatus, (*a*) in 10% acetic acid, pH 2·2, and (*b*) in pyridine–2N-acetic acid–water (1 : 5 : 80), pH 5·1. In each case Whatman no. 1 paper was used, and development was with 0·2% ninhydrin solution in butan-1-ol saturated with water, except where otherwise stated.

β-Benzyl Benzyloxycarbonyl-L-aspartate.—We have found it convenient to modify Berger and Katchalski's procedure [6] by using lithium hydroxide in aqueous acetone in place of sodium hydroxide in aqueous dioxan, a modification kindly communicated to us by Dr. D. F. Elliott. Dibenzyl benzyloxycarbonyl-L-aspartate (4·5 g.) was dissolved in aqueous acetone (1 : 4; 250 ml.), and a solution of lithium hydroxide (0·255 g.) in water (10 ml.) was added during ½ hr., with stirring at room temperature. The acetone was removed below 40° and unchanged diester was recovered by extraction into ether. The aqueous layer was acidified with 6N-hydrochloric acid, giving the β-ester as an oil, which soon crystallised. The product (2·5 g., 70%), after recrystallisation from benzene, had m. p. 107—109°, $[\alpha]_D^{17}$ +13·1° (*c* 10·0 in glacial acetic acid) (lit.,[6] m. p. 108°, $[\alpha]_D^{25}$ +12·1°).

Benzyloxycarbonyl-α-L-aspartyl-L-leucine Dibenzyl Ester.—(a) *Carbonic mixed anhydride method.*[7] β-Benzyl benzyloxycarbonyl-L-aspartate (5·34 g.) and dried triethylamine (2·1 ml.) were dissolved in toluene (30 ml.) and chloroform (10 ml.) at −5°; s-butyl chloroformate (2·0 ml.) was added dropwise with stirring, the temperature being kept at −5°. After 5 min., a similarly cooled solution of L-leucine benzyl ester toluene-*p*-sulphonate (7·07 g.) and triethylamine (2·4 ml.) in toluene (5 ml.) and chloroform (15 ml.) was added. The temperature was allowed to rise and the mixture was left overnight. The solution was washed with 2N-hydrochloric acid, N-potassium hydrogen carbonate, and water, dried ($MgSO_4$), and evaporated at reduced pressure. The residual oil slowly crystallised in the refrigerator; the solid was washed with light petroleum (b. p. 60—80°) and collected (3·65 g., 43·5%; m. p. 63—66°); recrystallisation from ether–light petroleum (b. p. 60—80°) and from ethanol–water gave *product* of m. p. 69·5—70·0°, $[\alpha]_D^{19}$ −22·5° (*c* 1·38 in acetone), $[\alpha]_D^{19}$ −29·8° (*c* 1·41 in ethanol) (Found: C, 68·5; H, 6·6; N, 5·35. $C_{32}H_{36}O_7N_2$ requires C, 68·5; H, 6·5; N, 5·0%).

(b) *Using ethylene phosphorochloridite (amide procedure* [8]). L-Leucine benzyl ester hydrochloride (2·36 g.) and triethylamine (1·6 ml.) were dissolved in diethyl phosphite (20 ml.). Ethylene phosphorochloridite [20] (0·54 ml.) was added, and the mixture was heated on a boiling-water bath for 5 min. β-Benzyl benzyloxycarbonyl-L-aspartate (2·14 g.) in diethyl phosphite (5 ml.) was added; after 1 hr. at 100°, the mixture was diluted with water, and the product which crystallised was collected and washed with water. Purification gave 1·66 g. (49%) of *product*, m. p. 68—68·5°.

α-L-Aspartyl-L-leucine.—Hydrogenation with palladium black of the product from coupling (*b*), in aqueous ethanol containing acetic acid, gave the *dipeptide*, which was recrystallised from aqueous acetone and dried at 100° for 12 hr. at 12 mm. (Found: C, 48·6; H, 7·4; N, 11·3. $C_{10}H_{18}O_5N_2$ requires C, 48·8; H, 7·3; N, 11·4%); it had $[\alpha]_D^{17}$ −10·6° (*c* 3·3 in water), $[\alpha]_D^{17}$ −9·7° (*c* 3·42 in 0·1N-hydrochloric acid), R_F in butanol–water–acetic acid, 0·60.

Tribenzyl Benzyloxycarbonyl-α-L-aspartyl-L-aspartate.—β-Benzyl benzyloxycarbonyl-L-aspartate (0·89 g.) was dissolved in dry methylene chloride (5 ml.), and a solution of dibenzyl L-aspartate toluene-*p*-sulphonate (m. p. 159—160°, 1·21 g.) and triethylamine (0·33 ml.) in methylene chloride (5 ml.), was added to it. Dicyclohexylcarbodi-imide (0·57 g.), in methylene chloride (20 ml.), was added to the mixture of esters. The solution was stirred for 6 hr., a few drops of glacial acetic acid were added (to decompose unchanged di-imide), and stirring was continued for a further ½ hr. Dicyclohexylurea, which had separated, was filtered off and the

[20] Lucas, Mitchell, and Scully, *J. Amer. Chem. Soc.*, 1950, **72**, 5491.

solvent was removed under reduced pressure, leaving a white solid. This was extracted into ethyl acetate (100 ml.) and washed successively with dilute hydrochloric acid, aqueous sodium hydrogen carbonate, and water. After drying ($MgSO_4$), the solvent was removed under reduced pressure and the product (1·36 g., 81%) was washed with light petroleum (b. p. 60—80°) and filtered off. After recrystallisation from absolute ethanol, the *product* had m. p. 108·5—109·5°, $[\alpha]_D^{16}$ +23·1° (*c* 5·0 in dry chloroform), $[\alpha]_D^{16}$ −6·1° (*c* 5·06 in acetone) (Found: C, 68·2; H, 5·6; N, 4·4. $C_{37}H_{36}O_9N_2$ requires C, 68·1; H, 5·6; N, 4·3%).

α-L-*Aspartyl*-L-*aspartic Acid*.—Tribenzyl benzyloxycarbonyl-α-L-aspartyl-L-aspartate in aqueous ethanol was hydrogenated in the presence of palladium black. The solution was filtered and the solvents were removed under a high vacuum. The sticky residue was washed with dimethylformamide, and the solid product (70%) was collected and dried. The crude material dissolved in the minimum of water, the solution filtered under gentle suction, and the solvent was removed under a high vacuum. The peptide was collected under absolute ethanol, filtered off, and dried at room temperature and 0·01 mm. for 6 hr. Further purification was effected by taking the peptide into water and adjusting the pH to 2; water was removed under a high vacuum and the product was collected under absolute ethanol as before, then having $[\alpha]_D^{20}$ +16·8° (*c* 5·0 in water), $[\alpha]_D^{20}$ +8·4° (*c* 5·0 in 0·5N-hydrochloric acid) (Found: C, 38·3; H, 5·4; N, 11·8. Calc. for $C_8H_{12}O_7N_2$: C, 38·7; H, 4·9; N, 11·3%), R_F in butanol–water–acetic acid 0·11, in phenol–water 0·05. After electrophoresis on paper, the movement relative to aspartic acid was 1·4 at pH 2·2, and 1·0 at pH 5·1.

Tribenzyl Benzyloxycarbonyl-α-L-*aspartyl*-L-*glutamate*.—The coupling procedure was identical with that described above, and the *product* was obtained as a white solid (78%). After recrystallisation from absolute ethanol it had m. p. 99—100°, $[\alpha]_D^{16}$ +12·5° (*c* 5·72 in dry chloroform), $[\alpha]_D^{15}$ −10·5° (*c* 5·25 in acetone) (Found: C, 68·8; H, 5·9; N, 4·4. $C_{38}H_{38}O_9N_2$ requires C, 68·5; H, 5·8; N, 4·2%).

α-L-*Aspartyl*-L-*glutamic Acid*.—Hydrogenation in aqueous methanol gave a product (85%) which was collected under absolute ethanol. After purification (as described for α-aspartylaspartic acid) it had m. p. 145—150° (lit., 150—155°,[2] 134—135° [15]), $[\alpha]_D^{18}$ +6·3° (*c* 5·0 in water), (lit., $[\alpha]_D^{25}$ +5·6° [2]; $[\alpha]_D^{19}$ −3·6° [15]), $[\alpha]_D^{18}$ +4·6° (*c* 5·0 in 0·5N-hydrochloric acid) (Found: C, 41·5; H, 5·4; N, 10·5. Calc. for $C_9H_{14}O_7N_2$: C, 41·2; H, 5·4; N, 10·7%), R_F in butanol–water–acetic acid 0·17, in phenol–water 0·04. After electrophoresis on paper, the movement relative to aspartic acid was 1·4 at pH 2·2, and 1·0 at pH 5·1.

α-*Benzyl* L-*Aspartate*.—55% Hydriodic acid was decolorised by dropping hypophosphorous acid into the boiling solution, and was then distilled. The constant-boiling hydriodic acid (8 ml.) so obtained was added to dibenzyl L-aspartate toluene-*p*-sulphonate (9·9 g.) dissolved in " AnalaR " glacial acetic acid (60 ml.), and the solution was kept at 45° for 29 hr. The solvent was then removed by distillation under reduced pressure. To remove traces of benzyl alcohol, small quantities of benzene were added to the residue in the flask and distilled off under reduced pressure. The dark, viscous residue was cooled to −10° and covered with absolute ethanol. Triethylamine (2·5 ml.) was added and the syrup triturated; slow dissolution of the dark material occurred with simultaneous deposition of yellow crystals. More triethylamine was added until the suspension had pH 7; it was then left in the refrigerator overnight. The solid (2·25 g., 50%) was collected, washed with alcohol and ether, and recrystallised from water, pH being adjusted to 5·5 with aqueous sodium hydroxide before filtration. The *product* had m. p. 174—175°, $[\alpha]_D^{18}$ −15·4° (*c* 5·0 in N-hydrochloric acid) (Found: C, 59·2; H, 5·9; N, 6·4. $C_{11}H_{13}O_4N$ requires C, 59·2; H, 5·9; N, 6·3%).

α-*Benzyl Benzyloxycarbonyl*-L-*aspartate*.—α-Benzyl L-aspartate (0·77 g.) and sodium hydrogen carbonate (0·8 g.) were dissolved in water (20 ml.) and stirred. Benzyl chloroformate (0·6 g.) was added dropwise, and stirring was continued for 5 hr. at room temperature. The aqueous solution was washed with ether, and concentrated hydrochloric acid was added to pH 2. An oil separated and was extracted into ethyl acetate. Solvent was removed under reduced pressure from the dried ($MgSO_4$) solution, and the sticky residue was left to crystallise under light petroleum (b. p. 60—80°). The product (70%) was recrystallised from toluene; it then had m. p. 84—85° (lit.,[11] 84—85°, 85°), $[\alpha]_D^{18}$ −9·7° (*c* 5·59 in acetic acid), $[\alpha]_D^{17}$ +8·8° (*c* 5·0 in dry chloroform), $[\alpha]_D^{17}$ −14·8° (*c* 5·0 in acetone) (Found: C, 63·8; H, 5·1; N, 4·0. Calc. for $C_{19}H_{19}O_6N$: C, 63·9; H, 5·3; N, 3·9%).

On two occasions, a considerable amount of a white solid separated during the reaction, and the isolated product had m. p. 109—111°. After several recrystallisations from toluene the

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m. p. of this material was raised to 116—116·5°, depressed on admixture with α-benzyl benzyloxycarbonyl-L-aspartate or with β-benzyl benzyloxycarbonyl-L-aspartate. The material absorbed strongly at 1801, 1719, 1672 cm.$^{-1}$ (in Nujol), in contrast with the authentic α-ester which had peaks at 1718 and 1658 cm.$^{-1}$ (Found: C, 66·0; H, 5·0; N, 4·1. Calc. for $C_{19}H_{19}O_6N$: C, 63·9; H, 5·3; N, 3·9. $C_{38}H_{36}O_{11}N_2$ requires C, 65·5; H, 5·2; N, 4·0%). After trituration of the crude material under sodium carbonate solution, the insoluble portion was filtered off and recrystallised once from toluene, then having m. p. 119—120°. This product was shown by infrared spectra (in Nujol and in chloroform), and by mixed melting point, to be identical with the material described below as *α-O-benzyl-N-benzyloxycarbonyl-β-L-aspartic anhydride.*

α-O-Benzyl-N-benzyloxycarbonyl-β-L-aspartic Anhydride.—α-Benzyl benzyloxycarbonyl-L-aspartate (m. p. 84—85°) was dissolved in acetic anhydride and left at room temperature overnight. The *product* was precipitated with light petroleum (b. p. 60—80°) and after recrystallisation from toluene had m. p. 120—121°, $[\alpha]_D^{17}$ +20·9° (*c* 5·0 in dry chloroform) (Found: C, 65·4; H, 5·2; N, 4·1%). It absorbed strongly at 1805, 1724, and 1678 cm.$^{-1}$ (in Nujol). A solution in glacial acetic acid containing a trace of water had $[\alpha]_D^{17}$ −9·8° (*c* 5·0), and a solution in moist acetone had $[\alpha]_D^{17}$ −14·9° (*c* 5·0). Material recovered from these solutions had m. p. 83—85°, confirming that hydrolysis had occurred in the moist solvents.

Tribenzyl Benzyloxycarbonyl-β-L-aspartyl-L-aspartate.—The coupling procedure was analogous to that described above for the α-isomer. The *product* (83%) was recrystallised from aqueous ethanol; it then had m. p. 121·5—123°, $[\alpha]_D^{16}$ +25·2° (*c* 5·0 in dry chloroform), $[\alpha]_D^{16}$ −5·7° (*c* 5·0 in acetone) (Found: C, 68·1; H, 5·7; N, 4·2. $C_{37}H_{36}O_9N_2$ requires C, 68·1; H, 5·6; N, 4·3%).

β-L-Aspartyl-L-aspartic Acid.—Hydrogenation in aqueous methanol gave a product (97%) which was collected under absolute ethanol. After purification (as described for α-aspartyl-aspartic acid) the *dipeptide* had $[\alpha]_D^{18}$ +4·8° (*c* 5·0 in water), $[\alpha]_D^{18}$ +18·2° (*c* 5·0 in 0·5N-hydrochloric acid) (Found: C, 39·0; H, 5·1; N, 11·4. $C_8H_{12}O_7N_2$ requires C, 38·7; H, 4·9; N, 11·3%), R_F in butanol–water–acetic acid 0·08, in phenol–water 0·06. After electrophoresis on paper, the movement relative to aspartic acid was 0·8 at pH 2·2, and 1·0 at pH 5·1.

Tribenzyl Benzyloxycarbonyl-β-L-aspartyl-L-glutamate.—The coupling procedure was analogous to that described above for the α-isomer. The *product* (87%), recrystallised from absolute ethanol, had m. p. 111·5—112·5°, $[\alpha]_D^{15}$ +10·7° (*c* 5·0 in dry chloroform), $[\alpha]_D^{15}$ −10·8° (*c* 5·25 in acetone) (Found: C, 68·7; H, 5·5; N, 4·3. $C_{38}H_{38}O_9N_2$ requires C, 68·5; H, 5·8; N, 4·2%).

β-L-Aspartyl-L-glutamic Acid.—Hydrogenation in aqueous methanol gave a product (79%) which was collected under absolute ethanol. After purification it had $[\alpha]_D^{18}$ −10·5° (*c* 5·25 in water), $[\alpha]_D^{18}$ +5·5° (*c* 5·05 in 0·5N-hydrochloric acid) (Found: C, 41·5; H, 5·4; N, 10·7. Calc. for $C_9H_{14}O_7N_2$: C, 41·2; H, 5·4; N, 10·7%), R_F in butanol–water–acetic acid 0·12, in phenol–water 0·07. After electrophoresis on paper, the movement relative to aspartic acid was 0·7 at pH 2·2, and 1·0 at pH 5·1.

α-(Benzyloxycarbonyl-α-L-aspartyl)-ε-benzyloxycarbonyl-L-lysine Dibenzyl Ester.—(*a*) *p-Nitrophenylthiolester procedure.*[16] β-Benzyl benzyloxycarbonyl-L-aspartate (0·89 g.) and 1-ethylpiperidine (0·34 ml.) were dissolved in anhydrous tetrahydrofuran. Ethyl chloroformate (0·24 ml.) was added dropwise to the vigorously stirred solution at 0°. After 15 min., *p*-nitrothiophenol (0·45 g.) in tetrahydrofuran was added, and the mixture was stirred for 4 hr. at room temperature. The solvent was removed under reduced pressure, and the product solidified under water at 5°. It was recrystallised from butan-1-ol (yield 1·0 g., 81%) and used directly. A small amount of 4,4′-dinitrodiphenyl disulphide (m. p. 177—178°) remained insoluble in the butanol.

The *α-p*-nitrophenyl β-benzyl benzyloxycarbonyl-α-thiol-L-aspartate (0·84 g.) thus prepared was dissolved in anhydrous tetrahydrofuran (10 ml.), and added to a mixture of ε-benzyloxycarbonyl-L-lysine benzyl ester hydrochloride (0·70 g.) and 1-ethylpiperidine (0·24 ml.), and the whole was heated under reflux for 2 hr. The solvent was removed under reduced pressure, and the residue was dissolved in chloroform and washed successively with water, 2N-hydrochloric acid, N-sodium hydrogen carbonate, and water. The chloroform solution was dried ($MgSO_4$) and filtered, and the solvent removed. Yellow crystals remained (1·2 g., 100%) which recrystallised from acetone–ether, yielding cream-coloured crystals (0·7 g., 60%), m. p. 116—117·5°.

Attempts to free the product from traces of 4,4′-dinitrodiphenyl disulphide by means of

bromine, potassium permanganate, hydrogen peroxide, or deactivated alumina, were not sufficiently effective to allow successful and reproducible catalytic hydrogenations to α-(α-L-aspartyl)-L-lysine.

(*b*) *Carbonic mixed anhydride method.*[7] β-Benzyl benzyloxycarbonyl-L-aspartate (2·55 g.) and triethylamine (1·0 ml.) were dissolved in anhydrous tetrahydrofuran and cooled to −5°. Isobutyl chloroformate (1·0 g.) was added dropwise with shaking, with protection against moisture. After 7 min., ε-benzyloxycarbonyl-L-lysine benzyl ester hydrochloride (2·90 g.) and triethylamine (1·20 ml.) in tetrahydrofuran were added. The mixture was allowed to reach room temperature slowly, and after 22 hr. was boiled under reflux for 1½ hr. The solvent was evaporated and replaced by ethyl acetate, and the solution was washed thoroughly with water, dilute hydrochloric acid, aqueous hydrogen carbonate, water, and brine. The ethyl acetate layer was dried ($MgSO_4$), filtered, and evaporated, leaving white crystals (3·1 g., 61%). The *product* recrystallised from acetone–di-isopropyl ether and had m. p. 116—117°. A further recrystallisation from methanol raised the m. p. to 118°, unchanged by further recrystallisation; $[\alpha]_D^{17}$ was −4·6° (*c* 3·5 in dioxan) (Found: C, 68·0; H, 6·2; N, 5·6. $C_{40}H_{43}O_9N_3$ requires C, 67·7; H, 6·1; N, 5·9%).

Couplings to form the above compound were attempted also by the ethylene phosphorochloridite " amide " and " standard " procedures, and through the phenyl thiolester. In all cases very low yields were obtained together with much unchanged starting materials. This was shown by hydrogenation of the crude products, followed by paper electrophoresis at pH 5·1, which gave three ninhydrin-positive spots, corresponding in position to aspartic acid, lysine, and the dipeptide respectively.

α-(*Benzyloxycarbonyl*-β-L-*aspartyl*)-ε-*benzyloxycarbonyl*-L-*lysine Dibenzyl Ester.*—(*a*) This compound was prepared by the procedure described for the α-isomer under (*a*) above. The crude product (75% yield) was considerably contaminated with 4,4′-dinitrodiphenyl disulphide, but after six recrystallisations from acetone–di-isopropyl ether, the colourless crystals had constant m. p. 153·5—154°, $[\alpha]_D^{17}$ −4·1° (*c* 2·93 in dioxan) (Found: C, 67·5; H, 6·3; N, 6·0%).

(*b*) This compound was also prepared by procedure (*b*) described for the α-isomer above. The product was obtained in 60% yield and after one recrystallisation had m. p. 153—154°, not depressed on admixture with the product obtained by method (*a*).

Hydrogenation of these α- and β-aspartyl derivatives, obtained by the carbonic mixed anhydride procedure, failed to give analytically pure dipeptides, although the products moved as single spots during paper electrophoresis at pH 5·1. Alternative methods of removing the benzyloxycarbonyl and the benzyl ester groups were tried. The use of sodium in liquid ammonia or hydrogen bromide in glacial acetic acid at 60° gave a by-product, which on paper electrophoresis at pH 5·1 moved as a cation and gave a bright yellow colour with ninhydrin; the dipeptides moved very slightly towards the cathode. The α-derivative gave a purple colour, and the β-derivative a blue colour, with ninhydrin.

Colour Reactions of α- *and* β-*Aspartyl-peptides.*—The following tests were applied to α- and β-aspartyl-L-valine, -L-tyrosine, -L-aspartic acid, and -L-glutamic acid, and to α-L-aspartyl-L-leucine. Aqueous solutions of the dipeptides (1%) were spotted on filter paper and treated with a 1% solution of ninhydrin in butan-1-ol or in ethanol, and the paper was *rapidly* dried at 100—120°. The α-aspartyl-peptides gave the normal purple colour, and the β-peptides a blue colour. Drying at lower temperatures gave various colours, usually shades of pink, instead of blue. With dilute aqueous copper sulphate and sodium hydroxide, solutions of the α-peptides gave a deep blue, and the β-isomers a pale blue colour (cf. ref. 19). Aqueous solutions of all the β-peptides dissolved copper carbonate to give a blue solution, as did α-aspartyl-aspartic and -glutamic acid; solutions of the remaining α-aspartyl-peptides failed to dissolve copper carbonate (cf. ref. 19).

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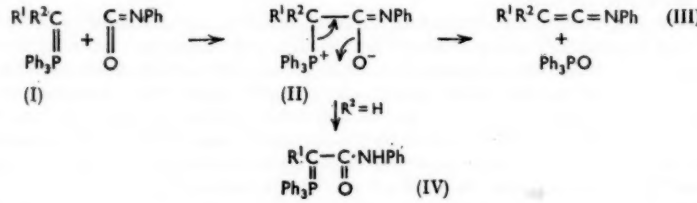
781. *The Reaction of Wittig Reagents with Phenyl Isocyanate.*

By S. Trippett and D. M. Walker.

The reaction of a series of Wittig reagents with phenyl isocyanate has been investigated. In general, the intermediate betaines rearranged to more stable Wittig reagents. Nitromethyltriphenylphosphonium bromide with aqueous alkali gave fulminic acid, and pyrolysis of the phosphorane (IX; $R^1 = R^2 = Ph$) gave diphenylacetylene.

The only recorded reaction of a Wittig reagent with phenyl isocyanate is that due to Staudinger and Meyer[1] who treated diphenylmethylenetriphenylphosphorane (I; R^1, $R^2 = Ph$) with phenyl isocyanate in boiling benzene and obtained 1,1-diphenyl-2-phenylimidoethylene (III; $R^1 = R^2 = Ph$). This may be formulated as a typical Wittig reaction proceeding *via* the betaine (II). It seemed probable that in similar betaines in which R^1 or R^2 was hydrogen, migration of that hydrogen to nitrogen would occur, to give a new Wittig reagent (IV), stabilised by resonance, which might then react with a further molecule of phenyl isocyanate. To investigate this possibility, the reaction of a series of Wittig reagents with phenyl isocyanate has been examined.



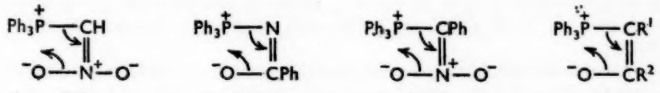
Methylenetriphenylphosphorane (I; $R^1 = R^2 = H$) with two molecules of phenyl isocyanate gave a betaine, stable to water, and shown to be di(phenylcarbamoyl)methylenetriphenylphosphorane (IV; $R^1 = CO{\cdot}NHPh$) by reduction with zinc and acetic acid to malondianilide; in this case, the Wittig reagent (IV; $R^1 = H$) formed by migration of one hydrogen atom reacted with a second molecule of phenyl isocyanate and gave a stable betaine by means of a second hydrogen transfer. Ethylidenetriphenylphosphorane (I; $R^1 = Me$, $R^2 = H$) consumed only one molecule of phenyl isocyanate; the resulting phosphorane (IV; $R^1 = Me$) decomposed in aqueous solution and was obtained as the corresponding quaternary bromide. Evidently one phenylcarbamoyl group is not sufficient to stabilise a Wittig reagent towards hydroxylic solvents. Isopropylidenetriphenylphosphorane (I; $R^1 = R^2 = Me$) gave the expected betaine (II; $R^1 = R^2 = Me$), isolated as the quaternary iodide.

Among the more stable Wittig reagents, ethoxycarbonylmethylenetriphenylphosphorane (I; $R^1 = CO_2Et$, $R^2 = H$) with one molecule of phenyl isocyanate gave the stable phosphorane (IV; $R^1 = CO_2Et$), whose structure was confirmed by the presence of NH absorption and by the absence of carbonyl absorption below 6 μ in the infrared spectrum. Similar stable phosphoranes were obtained from Wittig reagents in which $R^2 = H$, and $R^1 = CHO$, COMe, COPh, or CN. The phosphorane (I; $R^1 = CO{\cdot}NH_2$, $R^2 = H$) readily decomposed in hydroxylic solvents to triphenylphosphine oxide, and reacted with two molecules of isocyanate; it seems probable that the carbonyl group of the intermediate (IV; $R^1 = CO{\cdot}NH_2$) was sufficiently basic to react with a second molecule of phenyl isocyanate, giving the betaine (IV; $R^1 = CO{\cdot}NH{\cdot}CO{\cdot}NHPh$).

To complete this series of stable Wittig reagents, an attempt was made to prepare

[1] Staudinger and Meyer, *Ber.*, 1920, **53**, 72.

nitromethylenetriphenylphosphorane. However, an aqueous solution of nitromethyltriphenylphosphonium bromide at 0° with alkali gave an immediate quantitative precipitate of triphenylphosphine oxide. The solution contained fulminate ion, as shown by a positive test with ferrous–ferric ion (fulminate is reduced to cyanide by the ferrous ion [2]), the absence of nitromethane and of hypobromite ion, and the formation, after acidification with nitric acid, of a silver salt partly soluble in aqueous potassium chloride. The initially formed nitromethylenetriphenylphosphorane (VI) may have decomposed *via* a four-



(VI) (VII) (VIII) (IX)

membered state reminiscent of the Wittig reaction and analogous to the decomposition of benzoyliminotriphenylphosphorane (VII) above its melting point to triphenylphosphine oxide and benzonitrile.[3]

Horner *et al.*[4] suggested a similar scheme to account for the probable formation of benzonitrile oxide by the action of dichlorotriphenylphosphorane on phenylnitromethane in the presence of triethylamine, the phosphorane (VIII) being the supposed intermediate. In view of this, the action of heat on the stable phosphoranes (IX; $R^1 = H$, $R^2 = OEt$ or Me) was investigated, but in neither case was the expected acetylene detected. However, when α-benzoylbenzylidenetriphenylphosphorane (IX; $R^1 = R^2 = Ph$), prepared by the action of benzoyl chloride on benzylidenetriphenylphosphorane, was heated above its melting point, it gave triphenylphosphine oxide and diphenylacetylene quantitatively.

Experimental

Di(phenylcarbamoyl)methylenetriphenylphosphorane.—To a stirred suspension of methyltriphenylphosphonium bromide (3·7 g.) in ether (30 ml.) under nitrogen was added ethereal 1·4N-butyl-lithium (8 ml.), followed after 0·5 hr. by phenyl isocyanate (2·58 g.) in ether (10 ml.). After 0·5 hr., the ether was removed under reduced pressure and the residue crystallised from aqueous ethanol. Recrystallisation from butan-1-ol gave the *phosphorane*, m. p. 172—173° (decomp.) (Found: C, 76·8; H, 5·05; N, 5·3. $C_{33}H_{27}O_2N_2P$ requires C, 77·0; H, 5·3; N, 5·45%) Crystallisation from ethanol–dilute hydrochloric acid gave the quaternary *phosphonium chloride*, m. p. 207—209° (Found: C, 71·8; H, 5·0; N, 5·1. $C_{33}H_{28}O_2N_2PCl$ requires C, 71·9; H, 5·1; N, 5·1%).

The above phosphorane (1 g.) in chloroform (30 ml.) and acetic acid (20 ml.) was warmed with zinc dust (10 g.) until this had dissolved. Repeated washing of the resulting solution with water, followed by evaporation to low bulk, gave malondianilide, m. p. and mixed m. p. (from ethanol) 230—231° (Found: C, 70·9; H, 5·5; N, 11·3. Calc. for $C_{15}H_{14}O_2N_2$: C, 70·8; H, 5·5; N, 11·1%).

Triphenyl-α-phenylcarbamoylethylphosphonium Bromide.—To a stirred suspension of ethyltriphenylphosphonium bromide (3·5 g.) in ether (75 ml.) under nitrogen, was added ethereal 1·4N-butyl-lithium (9 ml.), followed after 1 hr. by phenyl isocyanate (1·2 g.) in ether (50 ml.). Evaporation of solvent under reduced pressure, and crystallisation of the residue from ethanol–dilute hydrobromic acid, gave the above quaternary *bromide*, m. p. 276—277° (Found: C, 66·6; H, 5·1; N, 2·95. $C_{27}H_{25}ONBr$ requires C, 66·2; H, 5·1; N, 2·9%).

In a similar way, isopropyltriphenylphosphonium iodide gave (*1-methyl-1-phenylcarbamoylethyl)triphenylphosphonium iodide*, m. p. (from ethanol) 276—278° (decomp.) (Found: C, 60·8; H, 4·9; N, 2·55. $C_{28}H_{27}ONPI$ requires C, 61·0; H, 4·9; N, 2·5%).

[α-Ethoxycarbonyl-α-(phenylcarbamoyl)methylene]triphenylphosphorane.—Ethoxycarbonylmethylenetriphenylphosphorane (3·5 g.) in chloroform (40 ml.) was treated with phenyl isocyanate (2 g.), and the solution set aside at room temperature for 2 hr. Solvent and excess

[2] Nef, *Annalen*, 1894, **280**, 330.
[3] Staudinger and Hauser, *Helv. Chim. Acta*, 1921, **4**, 861.
[4] Horner and Oediger, *Chem. Ber.*, 1958, **91**, 437.

of isocyanate were then removed at 100°/0·1 mm., and the residue crystallised from butan-1-ol to give the *phosphorane* (90%), m. p. 189—190° (Found: C, 74·35; H, 5·45; N, 2·9. $C_{29}H_{26}O_3NP$ requires C, 74·55; H, 5·5; N, 3·0%).

In a similar way, acetonylidenetriphenylphosphorane gave *α-phenylcarbamoylacetonylidenetriphenylphosphorane*, m. p. (from butan-1-ol) 191—192° (decomp.) (Found: N, 3·1. $C_{28}H_{24}O_2NP$ requires N, 3·2%); benzoylmethylenetriphenylphosphorane gave [*α-benzoyl-α-(phenylcarbamoyl)methylene*]*triphenylphosphorane*, m. p. (from chloroform–ethanol) 189° (decomp.) (Found: C, 80·05; H, 5·25; N, 3·0. $C_{35}H_{26}O_2NP$ requires C, 80·2; H, 5·0; N, 2·7%); and formylmethylenetriphenylphosphorane [5] gave [*α-formyl-α-(phenylcarbamoyl)methylene*]-*triphenylphosphorane*, m. p. (from ethanol) 230—231° (decomp.) (Found: N, 3·3. $C_{27}H_{22}O_2NP$ requires N, 3·3%).

α-Cyano-α-(phenylcarbamoyl)methylenetriphenylphosphorane.—Chloroacetonitrile (2 g.) and triphenylphosphine (5·2 g.) were dissolved in nitromethane (30 ml.), and the solution was refluxed for 5 hr. and cooled, to give *(cyanomethyl)triphenylphosphonium chloride*, m. p. 278—279°, $\lambda_{max.}$ 4·42 μ (Found: N, 4·0. $C_{20}H_{17}NPCl$ requires N, 4·15%). The chloride (1 g.) was dissolved in water (20 ml.) and the solution made alkaline with dilute sodium hydroxide solution, giving the *phosphorane*, m. p. (from ethyl acetate) 195—196°, $\lambda_{max.}$ 4·60 μ (Found: C, 79·7; H, 5·3; N, 4·45. $C_{20}H_{16}NP$ requires C, 79·7; H, 5·4; N, 4·65%).

This phosphorane (0·5 g.) in chloroform (10 ml.) was treated with phenyl isocyanate (1 g.) and refluxed for 2 hr. Removal of solvent and repeated crystallisation from butan-1-ol gave *α-cyano-α-(phenylcarbamoyl)methylenetriphenylphosphorane*, m. p. 205—206°, $\lambda_{max.}$ 4·55 μ (Found: N, 7·0. $C_{27}H_{21}ON_2P$ requires N, 6·7%).

Carbamoylmethylenetriphenylphosphorane.—Chloroacetamide (1·9 g.) and triphenylphosphine (5·2 g.) were refluxed in nitromethane (50 ml.) for 30 hr., then cooled, to give *carbamoylmethyltriphenylphosphonium chloride*, m. p. 227—229° (Found: N, 3·9. $C_{20}H_{19}ONPCl$ requires N, 3·94%). The chloride (1 g.) was dissolved in water (20 ml.) at 0° and made alkaline, and the precipitate filtered after not more than 1 min., washed rapidly with water, and dried, to give the *phosphorane*, m. p. 177—178° (Found: N, 4·45. $C_{20}H_{18}ONP$ requires N, 4·4%); this decomposed rapidly in contact with hydroxylic solvents.

The phosphorane (1 g.) was set aside with phenyl isocyanate (1 g.) in chloroform (10 ml.) at room temperature for 1 hr. Removal of solvent and crystallisation of the residue from ethanol gave [*α-phenylcarbamoyl-α-(N'-phenylureidocarbonyl)methylene*]*triphenylphosphorane* (IV; R^1 = CO·NH·CO·NHPh), m. p. 172—173° (Found: C, 73·0; H, 5·25; N, 7·45. $C_{34}H_{28}O_3N_3P$ requires C, 73·25; H, 5·1; N, 7·5%).

Nitromethyltriphenylphosphonium Bromide.—A solution of bromonitromethane (3·0 g.) in benzene (10 ml.) was slowly added to triphenylphosphine (5·2 g.) in benzene (20 ml.) at 0°, and the resulting solid filtered off and recrystallised from nitromethane, to give *nitromethyltriphenylphosphonium bromide*, m. p. 166° (decomp.) (Found: N, 3·7. $C_{19}H_{17}O_2NPBr$ requires N, 3·5%).

A solution of the bromide (1 g.) in water (20 ml.) at 0° was made alkaline and filtered after less than 1 min., to give triphenylphosphine oxide (0·65 g.), m. p. and mixed m. p. 157–158°.

α-Benzoylbenzylidenetriphenylphosphorane.—To a stirred suspension of benzyltriphenylphosphonium bromide (2·15 g.) in dry ether (100 ml.) under nitrogen was added ethereal 1·12N-butyl-lithium (4·4 ml.), and after 0·5 hr. the resulting solution added slowly to a stirred solution of benzoyl chloride (0·7 g.) in ether (50 ml.) under nitrogen. Evaporation of the ether and crystallisation of the residue from aqueous ethanol gave *α-benzoylbenzylidenetriphenylphosphorane* (0·6 g.), m. p. 191—192° (Found: C, 84·05; H, 5·5. $C_{32}H_{25}OP$ requires C, 84·2; H, 5·5%).

This phosphorane was heated at 300° for 0·5 hr. The distillate (b. p. ~250°) crystallised from aqueous ethanol to give diphenylacetylene, m. p. 58·5—59·5°, having the recorded ultraviolet spectrum.[6] The residue of triphenylphosphine oxide, washed with light petroleum, had m. p. and mixed m. p. 157—158°.

One of us (D. M. W.) acknowledges a maintenance grant from the Department of Scientific and Industrial Research.

THE UNIVERSITY, LEEDS, 2. [*Received, June 12th,* 1959.]

[5] Unpublished work.

[6] Friedel and Orchin, "Ultraviolet Spectra of Aromatic Compounds," J. Wiley and Sons, New York, 1951.

782. o-*Mercapto-azo-compounds. Part XII.* Preparation and Debenzylation of* 1-*Benzylthio*-2-o- *and* -p-*nitrophenylazonaphthalene.*

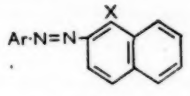
By A. Burawoy and S. S. Mistry.

The preparation and debenzylation of 1-benzylthio-2-*o*- and -*p*-nitrophenylazonaphthalene have been investigated. The preparation and properties of the corresponding 1-sulphenyl bromides, tribromides, iodides, thiocyanates, perchlorates, cyanides, the 1-sulphinic acids and 1-thiols, as well as of the disulphides and thiolsulphonates are reported.

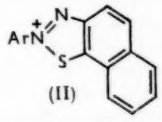
Our earlier investigation [1] of the debenzylation of 1-benzylthio-2-phenylazonaphthalene has been extended to its *o*- and *p*-nitrophenylazo-analogues (I; X = S·CH_2Ph) which are obtained in good yield by condensing 1-benzylthio-2-naphthylamine with *o*- and *p*-nitronitrosobenzene respectively in acetic acid. It is noteworthy that previous attempts to prepare azo-compounds of the naphthalene series by this method were unsuccessful.[2]

The *p*-nitro-derivative when heated with 1 and 2 mols. of bromine in acetic acid, gives almost quantitatively 2-*p*-nitrophenylazonaphthalene-1-sulphenyl bromide (I; X = SBr) and tribromide (I; X = SBr_3) respectively. The tribromide is only moderately stable; it dissociates into the sulphenyl bromide and bromine on crystallisation from nitrobenzene, acetic acid, or benzene and more slowly on storage at room temperature.

In contrast, the *o*-nitro-analogue yields only the sulphenyl tribromide (I; X = SBr_3), even when only 1 mol. of bromine is used (part of the starting material being then recovered). This is due to the exceptional stability of this tribromide which can be crystallised without decomposition from boiling nitrobenzene or acetic acid and dissociates in a vacuum only above 160° into bromine and 2-*o*-nitrophenylazonaphthalene-1-sulphenyl bromide (I; X = SBr). Indeed, this process is the best for preparation of the latter compound. The sulphenyl bromide crystallises as yellow needles with 2 mols. of water which are lost in a vacuum over phosphoric oxide, slowly at room temperature and rapidly at 100°, the crystals becoming orange. The process is reversed on exposure to air. This behaviour is similar to that observed for 4′-nitroazobenzene-2-sulphenyl thiocyanate.[3]



(I)



(II)

Ar = $NO_2·C_6H_4$

Both sulphenyl bromides and tribromides behave in other respects like the parent 2-phenylazonaphthalene-1-sulphenyl bromide and tribromide respectively. The sulphenyl bromides are stable to heat, soluble in water, and converted in aqueous solution by double decomposition with the corresponding potassium salts into the stable water-soluble iodides, thiocyanates, and perchlorates, as well as the water-insoluble cyanides. Except for the non-ionic cyanides, these water-soluble substances exist in the solid state and in solutions completely or partly as true salts of structure (II), involving a 2-*p*- or 2-*o*-nitrophenylnaphtho(2′, 1′ : 4, 5-)-1, 2, 3-thiadiazolium cation (see ref. 4).

The preparation and properties of the 2-*p*- and 2-*o*-nitrophenylazonaphthalene-1-sulphinic acids, as well as of the thiolsulphonates (disulphoxides), disulphides, monosulphides, and thiols are described in the Experimental section. Similar structures and properties of the corresponding parent substances have been discussed previously.[1,5]

* Part XI, *J.*, 1956, 653.

[1] Burawoy, Chaudhuri, and Hyslop, *J.*, 1956, 96.
[2] Zollinger, "Chemie der Azofarbstoffe," Birkhäuser Verlag, 1958, p. 114.
[3] Burawoy, Chaudhuri, and Vellins, *J.*, 1956, 90.
[4] Burawoy, Liversedge, and Vellins, *J.*, 1954, 4481.
[5] Burawoy and Chaudhuri, *J.*, 1956, 653.

XUM

Experimental

1-Benzylthio-2-o-nitrophenylazonaphthalene.—*o*-Nitronitrosobenzene (6·3 g.) in hot acetic acid (50 c.c.) was added to 1-benzylthio-2-naphthylamine (10 g.) in acetic acid (10 c.c.). The mixture was kept at room temperature overnight. The precipitate of almost pure *1-benzylthio-2-o-nitrophenylazonaphthalene* (10·5 g., 70%) was washed with a little acetic acid and light petroleum. Crystallisation from acetic acid gave red needles, m. p. 131—132° (Found: C, 69·1; H, 4·0; N, 10·3. $C_{23}H_{17}O_2N_3S$ requires C, 69·2; H, 4·3; N, 10·5%).

1-Benzylthio-2-p-nitrophenylazonaphthalene, similarly prepared (9·8 g., 65%), formed reddish-brown needles (from ethanol), m. p. 177—178° (Found: C, 69·2; H, 4·2; S, 8·2. $C_{23}H_{17}O_2N_3S$ requires C, 69·2; H, 4·3; S, 8·0%).

2-o-Nitrophenylazonaphthalene-1-sulphenyl Tribromide.—(i) 1-Benzylthio-2-*o*-nitrophenylazonaphthalene (5 g.), bromine (5 g., 2·5 mol.), and acetic acid (70 c.c.) were refluxed for 5 min. On cooling, almost pure *tribromide* separated (6·6 g., 95%). Crystallisation from nitrobenzene gave orange-yellow plates, m. p. 201—202° (decomp.) (Found: C, 35·3; H, 1·6; N, 7·9; S, 5·6. $C_{16}H_{10}O_2N_3SBr_3$ requires C, 35·1; H, 1·8; N, 7·7; S, 5·8%).

(ii) 1-Benzylthio-2-*o*-nitrophenylazonaphthalene (1 g.), bromine (0·42 g., 1 mol.), and acetic acid (15 c.c.) were refluxed for 30 min. After cooling, light petroleum (100 c.c.) was added and the precipitated oily product washed with more light petroleum till it solidified. The solid was extracted with benzene and the residue crystallised once from nitrobenzene, to give almost pure orange-yellow plates, m. p. 199—200° (decomp.) not depressed on addition of the pure tribromide prepared in the preceding experiment (0·4 g., 55%). Removal of the solvent from the benzene extract and crystallisation of the residue (0·1 g.) from acetic acid gave red needles, m. p. 131—132°, not depressed on addition of the starting material.

2-o-Nitrophenylazonaphthalene-1-sulphenyl Bromide.—2-*o*-Nitrophenylazonaphthalene-1-sulphenyl tribromide (10 g.) was heated in a vacuum at 160—165° until of constant weight (~3 hr.). The residual *sulphenyl bromide* crystallised from water as yellow needles, m. p. 261—262°, containing 2 mols. of water (Found: C, 45·6; H, 3·4; N, 10·2. $C_{16}H_{10}O_3N_3SBr,2H_2O$ requires C, 45·3; H, 3·3; N, 9·9%). On drying at 110° (P_2O_5) in a vacuum, the crystals lost the water and the colour changed to orange (Found: C, 49·1; H, 2·6; N, 10·8; S, 8·2. $C_{16}H_{10}O_3N_3SBr$ requires C, 49·5; H, 2·6; N, 10·8; S, 8·2%). On exposure to the atmosphere, the process was reversed.

2-p-Nitrophenylazonaphthalene-1-sulphenyl Bromide.—A solution of 1-benzylthio-2-*o*-nitrophenylazonaphthalene (6·5 g.) and bromine (3·12 g., 1·2 mol.) in acetic acid (80 c.c.) was refluxed for 15 min. On cooling, almost pure *sulphenyl bromide* separated in nearly quantitative yield. Crystallisation from water gave red needles, m. p. 257—258° (Found: C, 49·9; H, 2·9; N, 10·5. $C_{16}H_{10}O_3N_3SBr$ requires C, 49·5; H, 2·6; N, 10·8%).

2-p-Nitrophenylazonaphthalene-1-sulphenyl Tribromide.—The preceding experiment was repeated with 6·5 g. of bromine (2·5 mol.). The precipitate of the yellow-orange tribromide (86%) was filtered off, but dissociated slowly at room temperature and during drying into the monobromide and bromine. Crystallisation from solvents such as acetic acid or benzene gave pure monobromide.

The following derivatives were obtained almost quantitatively by the addition of potassium iodide, thiocyanate, perchlorate, and cyanide respectively to aqueous solutions of the sulphenyl bromides.

2-o-Nitrophenylazonaphthalene-1-sulphenyl iodide, dark brown needles (from water), m. p. 194—195°, soluble in water, ethanol, benzene, and chloroform with yellow, orange, green, and dark green colours respectively (Found: C, 44·2; H, 2·3; N, 9·7. $C_{16}H_{10}O_2N_3SI$ requires C, 44·1; H, 2·3; N, 9·6%). *2-p-Nitrophenylazonaphthalene-1-sulphenyl iodide*, red-brown needles (from water), m. p. 236—237° (colours in solution are similar to those of its *o*-nitro-isomer) (Found: C, 44·4; H, 2·3; N, 9·9%).

2-o-Nitrophenylazonaphthalene-1-sulphenyl thiocyanate, reddish-orange granules (from ethanol), m. p. 176—177° (decomp.) (Found: C, 55·5; H, 2·5; N, 15·1. $C_{17}H_{10}O_2N_4S_2$ requires C, 55·7; H, 2·7; N, 15·3%). para-*Isomer*, dark red plates (from ethanol), m. p. 212—213° (decomp.) (Found: C, 56·0; H, 3·0; N, 15·0%).

2-o-Nitrophenylazonaphthalene-1-sulphenyl cyanide (*1-thiocyanato-2-o-nitrophenylazonaphthalene*), yellow needles (from benzene–light petroleum), m. p. 185—186° (Found: C, 61·8; H, 3·0; N, 16·5. $C_{17}H_{10}O_2N_4S$ requires C, 61·2; H, 3·0; N, 16·8%). para-*Isomer*, red needles (from benzene), m. p. 196—197° (Found: C, 61·5; H, 3·1; N, 16·7%).

2-o-*Nitrophenylazonaphthalene*-1-*sulphenyl perchlorate*, yellow plates (from nitrobenzene), m. p. 274—275° (decomp.) (Found: C, 47·7; H, 2·7; N, 10·4. $C_{16}H_{10}O_6N_3SCl$ requires C, 47·1; H, 2·5; N, 10·3%). para-*Isomer*, orange-yellow needles (from water), m. p. 283—284° (decomp.) (Found: C, 47·0; H, 2·7; N, 10·4%).

Di-(2-o-*nitrophenylazo*-1-*naphthyl*) *Disulphide*.—A suspension of 2-*o*-nitrophenylazonaphthalene-1-sulphenyl bromide (0·5 g.) and zinc dust (4 g.) in benzene (50 c.c.) was refluxed for 10 min., then filtered whilst hot and evaporated. The residual *disulphide* (0·35 g., 88%) crystallised from benzene–light petroleum as red needles, m. p. 220—221° (Found: C, 62·7; H, 3·3; S, 10·4. $C_{32}H_{20}O_4N_6S_2$ requires C, 62·3; H, 3·3; S, 10·4%). A similar result was obtained on treatment of the sulphenyl tribromide with zinc dust for a longer period.

Di-(2-p-*nitrophenylazo*-1-*naphthyl*) *Disulphide*.—A suspension of the sulphenyl bromide (1·5 g.) and zinc dust (10·5 g.) in benzene (150 c.c.) was refluxed for 30 min. and worked up as in the preceding experiment (yield 0·8 g., 67%). Crystallisation as before gave dark brown needles, m. p. 234—235° (Found: C, 62·6; H, 3·4%).

2-o-*Nitrophenylazonaphthalene*-1-*sulphinic Acid*.—An excess of 10% aqueous sodium hydroxide (10 c.c.) was added to a suspension of the tribromide (0·5 g.) in ethanol (50 c.c.). The resultant deep red solution was diluted with cold water (200 c.c.) and, after filtration, acidified with dilute hydrochloric acid. The precipitated *sulphinic acid* was washed with a small amount of water and with light petroleum (0·3 g., 90%). Crystallisation from benzene gave yellow prisms, m. p. 168—169° (decomp.) (Found: C, 56·5; H, 3·2; N, 12·7. $C_{16}H_{11}O_4N_3S$ requires C, 56·3; H, 3·2; N, 12·3%).

The acid at its m. p. and in ethanol, methanol, or chloroform solution, slowly at room temperature and rapidly when heated, dissociated into 2-o-*nitrophenylazonaphthalene* and sulphur dioxide. Crystallisation from ethanol gave reddish-brown needles, m. p. 100—101° (Found: C, 69·4; H, 3·9; N, 15·4. $C_{16}H_{11}N_3O_2$ requires C, 69·3; H, 4·0; N, 15·2%).

The para-*isomer* was obtained similarly by action of sodium hydroxide on freshly prepared sulphenyl tribromide without prior drying and crystallisation. Crystallisation from benzene gave white needles, m. p. 193—194° (Found: C, 56·3; H, 3·2%). Its behaviour is analogous to that of the *o*-nitro-isomer. 2-p-*Nitrophenylazonaphthalene* crystallised from light petroleum (b. p. 60—80°) as red needles, m. p. 196—197° (Found: C, 69·2; H, 3·9%).

Di-(2-o-*nitrophenylazo*-1-*naphthyl*) *Sulphide and the Derived Thiolsulphonate*.—2-*o*-Nitrophenylazonaphthalene-1-sulphinic acid (0·5 g.) was dissolved in warm water (350 c.c.) containing sodium hydroxide (0·058 g., 1 mol.). The solution, after cooling, was added to 2-*o*-nitrophenylazonaphthalene-1-sulphenyl bromide (0·5 g.) in water (400 c.c.) with stirring. The dark-orange precipitate of the crude thiolsulphonate was quickly filtered off. It decomposes slowly at room temperature or rapidly when heated into the sulphide and sulphur dioxide (Found for crude disulphoxide: C, 58·1; H, 3·1; N, 13·3. Calc. for $C_{32}H_{20}O_6N_6S_2$: C, 59·2; H, 3·1; N, 13·0%). Crystallisation from benzene gave red-brown prisms of the *monosulphide*, m. p. 275—276° (decomp.) (Found: C, 65·3; H, 3·3; N, 14·3. $C_{32}H_{20}O_4N_6S$ requires C, 65·7; H, 3·4; N, 14·4%).

The analogous *p*-nitro-thiolsulphonate, when crystallised from benzene, yielded deep red plates of the *sulphide*, m. p. 268—269° (Found: C, 65·5; H, 3·5%).

Action of Sodium Hydroxide (*Excess*) *on* 2-o-*Nitrophenylazonaphthalene*-1-*sulphenyl Bromide*.—10% Aqueous sodium hydroxide (20 c.c.) was added to a solution of the sulphenyl bromide (2 g.) in water (300 c.c.). The precipitate of disulphide was collected (0·9 g., 85%). Crystallisation from benzene and light petroleum gave dark red crystals, m. p. 220—221°, not depressed on addition of the disulphide obtained by the action of zinc. The alkaline filtrate was acidified with dilute hydrochloric acid, and the pink precipitate consisting almost exclusively of the sulphinic acid was filtered off and washed with water (0·5 g., 86%). Crystallisation from benzene gave yellow prisms, m. p. and mixed m. p. 168—169°.

Results with the *para*-isomer were similar.

Action of Sodium Hydrogen Carbonate (1 *Mol.*) *on* 2-o-*Nitrophenylazonaphthalene*-1-*sulphenyl Bromide*.—A solution of sodium hydrogen carbonate (0·084 g.) in water (1 c.c.) was added to the sulphenyl bromide (0·4 g.) in water (250 c.c.). After 3 hours' stirring, the precipitate consisting of the disulphide, thiolsulphonate, and/or sulphide, was collected, washed with water, and dried (0·3 g.). The mixture was suspended in ethanol (20 c.c.) and refluxed for 4 min. with a solution of sodium sulphide nonahydrate (0·3 g.) in 5% aqueous sodium hydroxide (4 c.c.). After addition of water, the insoluble monosulphide (0·1 g.) was collected. Crystallisation from

benzene gave dark red prisms, m. p. and mixed m. p. 275—276°. The filtrate was acidified with dilute hydrochloric acid. The precipitate of thiol (see below) was collected (~0·1 g.). Crystallisation from benzene gave red needles of disulphide, m. p. and mixed m. p. 220—221°.

In another experiment, the mixture of the disulphide and monosulphide was separated by a more tedious fractional crystallisation from benzene, the monosulphide being much less soluble than the disulphide. Pure specimens were obtained in moderate yields.

1-*Mercapto*-2-o-*nitrophenylazonaphthalene*.—A solution of sodium sulphide nonahydrate (0·4 g.) in 5% aqueous sodium hydroxide (8 c.c.) was added to a suspension of the disulphide (0·6 g.) in ethanol (70 c.c.). The mixture was refluxed for 5 min. After cooling and addition of oxygen-free water (70 c.c.), the dark reddish-brown solution was filtered and acidified with hydrochloric acid. The precipitated crude 1-*mercapto*-2-o-*nitrophenylazonaphthalene* was quickly collected, washed with water, and dried (P_2O_5) (0·4 g., 66%; m. p. 105—115°) (Found: C, 62·2; H, 3·5; N, 14·6. $C_{16}H_{11}O_2N_3S$ requires C, 62·1; H, 3·6; N, 13·6%). On storage its solubility in ethanolic sodium hydroxide decreased and its m. p. rose (*e.g.*, 138—145° after 3 days; 170—180° after 3 weeks). Crystallisation from benzene and light petroleum yielded, in spite of precautions to exclude oxygen, red needles of the disulphide, m. p. and mixed m. p. 220—221°. The experiment was repeated with half the quantities, but 10% aqueous sodium hydroxide (10 c.c.) and benzyl chloride (2 c.c.) were added with stirring to the filtered red solution. The mixture was heated on a water-bath for 1 hr. and set aside for 20 hr. The precipitate of 1-benzylthio-2-o-nitrophenylazonaphthalene was collected (0·35 g., 88%). Crystallisation from acetic acid gave red needles, m. p. and mixed m. p. 131—132°.

The same product (0·1 g., 50%) was obtained by heating, on a water-bath, a filtered solution of freshly prepared crude 1-mercapto-2-o-nitrophenylazonaphthalene (0·15 g.) in ethanol (25 c.c.) and 10% aqueous sodium hydroxide (10 c.c.) with benzyl chloride (1 c.c.), with subsequent addition of water.

1-*Mercapto*-2-p-*nitrophenylazonaphthalene*.—Reduction of the disulphide (0·4 g.) carried out as for the o-nitro-isomer yielded the *thiol* (0·2 g., ~50%; m. p. 90—98° immediately after separation, 110—120° after 24 hr. and 195—210° after 5 days). Crystallisation from benzene and light petroleum gave brown needles of the disulphide, m. p. and mixed m. p. 234—235°. In another experiment, treatment of the filtered solution with benzyl chloride yielded 1-benzylthio-2-*p*-nitrophenylazonaphthalene (80%), red needles (from acetic acid), m. p. and mixed m. p. 177—178°. The same product (0·04 g., 31%) was obtained on benzylation of an alkaline solution of freshly isolated crude thiol (0·1 g.).

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783. *The Chemotherapy of Schistosomiasis. Part III.** N-p-*Aminophenoxyalkyl-amides, -imides, and -sulphonamides.*

By J. N. ASHLEY, R. F. COLLINS, M. DAVIS, and N. E. SIRETT.

Many acyl- and diacyl-aminoalkyl ethers of *p*-aminophenol have been prepared by a number of routes. Some of these compounds are effective schistosomicides.

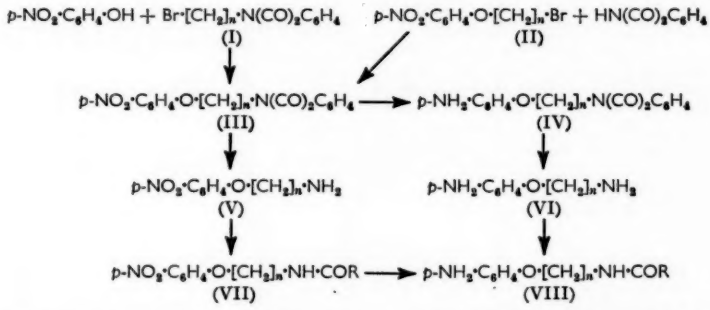
AFTER the discovery (see Part II *) that many simple ethers of *p*-aminophenol were curative against *S. mansoni* infections in mice, some basic alkyl ethers were examined. These were ineffective, but an intermediate in their preparation, 1-*p*-aminophenoxy-5-phthalimidopentane (IV; $n = 5$), showed high activity. This unexpected result led us to prepare a large number of related amides, imides, and sulphonamides, some of which are now reported. Many others have been briefly described in patent specifications [1] and are therefore omitted from this paper. The biological results will be published elsewhere.[2]

* Part II, Ashley, Collins, Davis, and Sirett, *J.*, 1959, 897.

[1] May and Baker Ltd., B.P. 769,706; 778,919; 808,952.

[2] Collins, Davis, Edge, and Turnbull, *J. Pharm. Pharmacol.*, 1959, in the press.

The homologous series of 1-*p*-nitrophenoxy-ω-phthalimidoalkanes (III) was prepared (as far as the decane) by condensing the appropriate ω-phthalimidoalkyl bromide (I) with potassium *p*-nitrophenoxide. Catalytic reduction over Raney nickel afforded the amines (IV) in high yield. All the amines in this series formed bright yellow crystals giving almost colourless, dilute solutions in organic solvents, from which they were precipitated initially in a colourless amorphous form which became yellow as crystallisation set in. Reduction of the nitro-group of the ether (III) over platinum oxide under pressure invariably resulted in some reduction of the phthalimide ring. In one case, when the reduction was allowed to proceed to completion, the hexahydro-derivative (IXc) was isolated in good yield. The phthalimide base (IV; $n = 5$) with tin and hydrochloric acid gave the phthalimidine (Xc).



An alternative method used for the preparation of the phthalimide (III; $n = 5$) and for the analogous camphorimide, phthalylhydrazide, 2-pyridone, thiazolidine-2,4-dione, 2,3-dihydro-3-oxobenzisothiazole, butane-1,4-sultam, and naphthalene-1,8-sultam derivatives was the reaction of 5-*p*-nitrophenoxypentyl bromide (II) or iodide with the appropriate cyclic amide or imide. In the case of 2,3-dihydro-3-oxobenzisothiazole (XI; R = H), condensation of the sodium salt with 5-*p*-nitrophenoxypentyl bromide in 2-ethoxyethanol gave the *N*-alkylated derivative (XIa), the structure of which was confirmed by oxidation with hydrogen peroxide to the known saccharin compound (XIIa).[1] However, when the condensation was effected by using potassium carbonate in acetone, the product was an isomer of (XIIa), probably the *O*-ether (XIIIa). Both *N*- and *O*-alkyl-2,3-dihydro-3-oxobenzisothiazoles are known.[3] Since chemical reduction of the nitro-group also appeared to rupture the heterocyclic ring,[4] the acetamido-derivative (XIb) was made from 5-*p*-acetamidophenoxypentyl bromide and was hydrolysed with acid to the required amine (XIc).

In a third route employed for the 3-nitrophthalimide, tetrachlorophthalimide, and homophthalimide analogues of (III; $n = 5$), the phthalimide was hydrolysed with hydrazine to 1-amino-5-*p*-nitrophenoxypentane (V; $n = 5$) which was fused with the appropriate cyclic anhydride. 5-Amino-1-*p*-nitrophenoxypentane served also as an intermediate for the preparation of a large number of aliphatic, aromatic, and heterocyclic amides (VII; $n = 5$) and sulphonamides, most of which were made by standard acylation procedures.[1] The maleamic acid (VII; $n = 5$; R = CH:CH·CO_2H) obtained from nitro-amine (V; $n = 5$) and maleic anhydride was cyclised to the maleimide by acetic anhydride and sodium acetate,[5] and the nitro-group was reduced with stannous chloride. The maleimide ring of the base obtained was very sensitive to alkali, readily opening to give the maleamic acid (VIII: $n = 5$; R = CH:CH·CO_2H). The analogous glutaramic acid (XVa; R′ = H), similarly prepared, was best cyclised to the imide (XVIa) by acetyl chloride.[6] When

[3] Reissert and Manns, *Ber.*, 1928, **61**, 1308.
[4] McClelland and Gait, *J.*, 1926, 923; McKibben and McClelland, *J.*, 1923, 172.
[5] Du Pont, U.S.P. 2,444,536.
[6] Henbest and Owen, *J.*, 1955, 2968.

TABLE 1. *Nitro-amides*, p-R·C_6H_4·O·$[CH_2]_n$·NHR'.

n	R	R'	Yield (%)	M. p.	Recryst. from	Formula	Found (%) C	H	N		Required (%) C	H	N	
4	NO_2	Bz	82	102—103°	Aq.AcOH	$C_{17}H_{18}O_4N_2$	65·5	6·0	9·2		64·9	5·7	8·9	
5	NO_2	p-Br·C_6H_4·CO	81	153—154	EtOH	$C_{18}H_{19}O_4N_2Br$			6·7	19·1 [a]			6·9	19·6 [a]
5	NO_2	p-Me·C_6H_4·CO	73 [b]	132—133	AcOH	$C_{19}H_{22}O_4N_2$	66·65	6·5	8·0		66·7	6·5	8·2	
5	NO_2	p-NO_2·C_6H_4·CO	49 [b]	148—150	$COMe_2$	$C_{18}H_{19}O_6N_3$			11·4				11·25	
5	NO_2	p-AcO·C_6H_4·CO	54	131—133	$COMe_2$	$C_{20}H_{22}O_6N_2$	62·0	5·9	7·1		62·1	5·7	7·25	
5	NO_2	p-HO·C_6H_4·CO	91 [c]	147—150	PhMe	$C_{18}H_{20}O_5N_2$	62·5	5·7	8·4		62·8	5·8	8·15	
5	NO_2	o-CO_2Me·C_6H_4·CO	61	140—141	C_6H_6	$C_{20}H_{22}O_6N_2$	62·2	5·3	7·2		62·1	5·7	7·25	
5	NO_2	p-CO_2Me·C_6H_4·CO	56	164—166	EtOH	$C_{20}H_{22}O_6N_2$	62·0	5·95	7·45		62·1	5·7	7·25	
5	NO_2	p-Me·SO_2·C_6H_4·CO	22 [d]	169—171	AcOH	$C_{19}H_{22}O_6N_2S$	56·3	5·8	6·6		56·2	5·4	6·9	
5	NO_2	Hexahydrobenzoyl	87	123	AcOH	$C_{18}H_{26}O_4N_2$	64·4	7·9	8·3		64·6	7·8	8·6	
5	NO_2	Et·CO	69	79—80	Aq. EtOH	$C_{14}H_{20}O_4N_2$			10·05				10·0	
5	NO_2	n-C_5H_{11}·CO	60	59—60	Et_2O	$C_{17}H_{26}O_4N_2$	63·4	8·3	8·8		63·4	8·1	8·7	
5	NO_2	Ph_2CH·CO	53	104—106	Aq. $COMe_2$	$C_{25}H_{26}O_4N_2$	71·4	6·1	6·9		71·7	6·3	6·7	
5	NO_2	Ph·$[CH_2]_4$·CO	82	87—89	Aq. EtOH	$C_{22}H_{28}O_4N_2$			7·3				7·3	
5	NO_2	2,4-$Cl_2C_6H_3$·O·CH_2·CO	37	112—114	EtOH	$C_{19}H_{20}O_6N_2Cl_2$			6·5	16·3 [e]			6·55	16·6 [e]
5	NO_2	$C_6H_4(CO)_2N$·CH_2·CO	68	183·5—185	EtO·$[CH_2]_2$·OH	$C_{21}H_{21}O_6N_3$			9·95				10·2	
5	AcNH	p-NO_2·C_6H_4·CO		214—217·5	EtOH or EtO·$[CH_2]_2$·OH	$C_{20}H_{23}O_5N_3$	62·3	5·6	10·9		62·3	6·0	10·9	
8	NO_2	Ph·SO_2	71	73—75	EtOH	$C_{20}H_{26}O_6N_2S$			6·8	8·25 [f]			6·9	7·9 [f]
5	NO_2	p-Me·C_6H_4·SO_2	93	154—156	Aq. EtOH	$C_{18}H_{22}O_6N_2S$			7·8				7·4	
5	NO_2	p-NHAc·C_6H_4·SO_2	77	129—131	Aq. EtOH	$C_{19}H_{23}O_6N_3S$			9·7	7·9 [f]			10·0	7·6 [f]

[a] Br. [b] Overall from the phthalimide. [c] Prepared by alkaline hydrolysis of the acetoxy-derivative. [d] Overall from carboxylic acid. [e] Cl. [f] S.

TABLE 2. *Compounds*, p-NH_2·C_6H_4·O·$[CH_2]_n$·R.

n	R	Derivative	Yield (%)	M. p.	Recryst. from	Formula	Found (%) C	H	N	S	Required (%) C	H	N	S
2	Phthalimido	Base	59	159—160°	EtOH	$C_{16}H_{14}O_3N_2$			9·6				9·9	
		Me·SO_3H		198—199		$C_{16}H_{14}O_3N_2,CH_4O_3S$			7·2				7·4	
3	Phthalimido	Base	94	67—68 or 92—93 [a]	$CHCl_3$–Et_2O	$C_{17}H_{16}O_3N_2$	69·1	5·75	9·4		68·9	5·4	9·4	
		Me·SO_3H		163—165	EtOH–Et_2O	$C_{17}H_{16}O_3N_2,CH_4O_3S$			7·1				7·1	
4	Phthalimido	Base	59	124—125	EtOH	$C_{18}C_{18}O_3N_2$	69·2	5·7	8·9		69·6	5·8	9·0	
10	Phthalimido	Base	70	98	EtOH	$C_{24}H_{30}O_3N_2$	73·1	7·8	7·1		73·1	7·6	7·1	
5	Tetrachlorophthalimido	Base	55	180—182	2-Ethoxyethanol	$C_{19}H_{16}O_3N_2Cl_4$			6·1 [b]				6·05	
5	3-Nitrophthalimido	Base	30 [c]	117—118	EtOH	$C_{19}H_{19}O_5N_3$			10·95				11·35	
		Me·SO_3H		183—185	EtOH–Et_2O	$C_{19}H_{19}O_5N_3,CH_4O_3S$			8·8	7·05			9·0	6·9
5	3-Aminophthalimido	Base	87	105—107	EtOH	$C_{19}H_{21}O_3N_3$	66·85	6·6	12·2		67·25	6·2	12·4	
5	Homophthalimido	Me·SO_3H	85	187—189	MeOH	$C_{20}H_{22}O_3N_2,CH_4O_3S$	58·4	6·2	6·55		58·0	6·0	6·45	
5	3,4-Dihydro-2,4-dioxo-5,6-benz-1,3-oxazin-3-yl	Base	95	136—138	EtOH	$C_{19}H_{20}O_4N_2$	67·25	6·25	8·1		67·0	5·9	8·2	
5	Camphorimido	$0·5H_2SO_4$	54	183—185	EtOH–Et_2O	$C_{21}H_{30}O_3N_2,0·5H_2SO_4$			7·1	4·0			6·9	3·9
5	1,2,3,4-Tetrahydro-1,4-dioxo-phthalazin-2-yl	Base	43	169—171	EtOH	$C_{19}H_{21}O_3N_3$	67·15	6·4	12·25		67·25	6·2	12·4	

TABLE 2. (*Continued.*)

n	R	Derivative	Yield (%)	M. p.	Recryst. from	Formula	Found (%) C	H	N	S	Required (%) C	H	N	S
5	Glutarimido	Base	93	109	EtOH	$C_{16}H_{22}O_3N_2$	65·85	7·75	9·8		66·2	7·6	9·2	
5	β-Ethyl-β-methylglutarimido	Base	57 [e]	99—100	C_6H_6	$C_{19}H_{28}O_3N_2$	68·7	8·25	8·4		68·6	8·4	8·4	
5	Hexahydro-2,4,6-trioxopyrimidin-1-yl	Base	78	211—214 (efferv.)	NMe_2·CHO–EtOH	$C_{12}H_{19}O_4N_3$	59·05	6·3	13·7		59·0	6·2	13·8	
4	α-Phthalimidobenzyl	Base	73	112—113	EtOH	$C_{25}H_{24}O_3N_2$	75·0	6·1	7·0		75·0	6·0	7·0	
4	α-Benzamidobenzyl	$Me·SO_3H$	63	177—179	EtOH–Et_2O	$C_{24}H_{26}O_5N_2S$, CH_4O_3S			5·8	7·2			6·0	6·8
5	NH·CHO	Base	89	74—76	C_6H_6	$C_{12}H_{16}O_2N_2$	65·1	8·3	12·4		64·9	8·1	12·6	
5	NH·COEt	Base	70	77·5—79	C_6H_6	$C_{14}H_{32}O_2N_2$	67·1	11·1	8·8		67·2	11·2	8·8	
		CHPh:		122·5—123·5		$C_{21}H_{26}O_2N_2$			8·3				8·3	
5	NH·CO·C_6H_{11}-n	Base	74	86—87	EtOH–Et_2O	$C_{17}H_{32}O_2N_2$	69·8	10·0	9·8		69·8	9·6	9·6	
5	NH·CO·$[CH_2]_4$·Ph	Base	87	92	$CHCl_3$–Pet [e]	$C_{22}H_{30}O_2N_2$			7·95				7·9	
5	NH·CO·CO_2Et	Base	85	78—80	$CHCl_3$–Pet	$C_{15}H_{22}O_4N_2$	61·25	7·25	9·7		61·2	7·5	9·5	
		$Me·SO_3H$		142—143	EtOH–Et_2O	$C_{15}H_{22}O_4N_2$, CH_4O_3S			7·2	8·3			7·2	8·2
5	NH·CO·$CHPh_2$	Base	80	101—102·5	EtOH–Pet	$C_{25}H_{28}O_2N_2$	76·8	7·1	7·3		77·25	7·3	7·2	
5	NH·CO·CH_2·$C_6H_2Cl_2$-1,2,4	Base	84	104·5—106·5	EtOH	$C_{19}H_{22}O_3N_2Cl_2$			7·1 [f]				7·05	
5	NH·CO·CH_2·$N(CO)_2$·C_6H_4-*o*	Base	98	156·5—158·5	EtOH	$C_{21}H_{23}O_4N_3$			11·1				11·1	
5	NH·CO·CH_2·NH·COPh	Base	81	119—121	EtOH	$C_{20}H_{25}O_3N_3$	67·6	7·4	11·7		67·6	7·1	11·8	
5	Pantothenamido	Base	86	[g]		$C_{20}H_{33}O_5N_3$, $0·5C_2H_5·OH$	60·6	9·0	10·1		60·2	8·7	10·0	
5	Hexahydrobenzamido	Base	85	103—104	C_6H_6	$C_{18}H_{28}O_2N_2$	71·4	9·3	9·2		71·0	9·2	9·2	
5	$N(COPh)_2$	Base	87	92—93	EtOH	$C_{28}H_{26}O_3N_2$	74·6	6·4	6·75		74·6	6·6	6·95	
4	NH·COPh	Base	80	108	EtOH	$C_{17}H_{20}O_2N_2$	72·0	7·25	9·6		71·9	7·05	9·85	
5	NH·CO·C_6H_4Me-*p*	Base	84	123—124	$CHCl_3$–Pet	$C_{19}H_{24}O_2N_2$	73·35	7·7	8·85		73·1	7·75	8·95	
5	NH·CO·C_6H_4Br-*p*	Base	47	118—120	EtOH	$C_{18}H_{21}O_2N_2Br$	57·4	5·6	7·6		57·3	5·6	7·4	
		CHPh:		154—155	EtOH	$C_{25}H_{25}O_2N_2Br$			5·95				5·9	
5	NH·CO·C_6H_4·OH-*p*	Base	67	192·5—194	EtOH	$C_{18}H_{22}O_3N_2$	68·4	7·1	8·6		68·8	7·0	8·9	
5	NH·CO·C_6H_4·OH-*o*	Base	80	122—123	Aq. MeOH	$C_{18}H_{22}O_3N_2$	68·7	7·2	8·7		68·8	7·0	8·9	
5	NH·CO·C_6H_4·CO_2Me-*p*	Base	77	141—143	PhMe	$C_{20}H_{24}O_4N_2$	67·8	6·7	8·0		67·5	6·75	7·9	
5	NH·CO·C_6H_4·CO_2H-*p*	Base	93 [h]	242—244 [i]	Aq. H·CO·NMe_2	$C_{19}H_{22}O_4N_2$	67·1	6·95	8·6		66·7	6·4	8·2	
5	NH·CO·C_6H_4·SO_2Me-*p*	Base	77	144—145	EtOH	$C_{19}H_{24}O_4N_2S$	60·35	6·45	7·2		60·6	6·4	7·4	
5	NH·CO·C_6H_4·NO_2-*p*	Base	75 [b]	139—141	EtOAc	$C_{18}H_{21}O_4N_3$	63·1	6·1	12·2		63·0	6·1	12·25	
5	NH·CO·C_6H_4·NHAc-*p*	Base	89	173·5—174·5	EtOH	$C_{20}H_{25}O_3N_3$	67·5	6·9	11·9		67·6	7·1	11·8	
5	NH·CO·C_6H_4·NH_2-*p*	Base	80	121—123	EtOH	$C_{18}H_{23}O_2N_3$			13·4				13·2	
		2Me·SO_3H		272—274 [i]	EtOH–Et_2O	$C_{18}H_{23}O_2N_3$, $2CH_4O_3S$			8·3				8·3	
5	NPh·COMe	Base	62 [j]	66—68	Et_2O–Pet	$C_{19}H_{24}O_2N_2$	72·9	7·4	8·9		73·1	7·7	9·0	
5	*N*-Cyclohexylbenzamido	Base	80	72—75	Et_2O–Pet	$C_{24}H_{32}O_2N_2$			7·2				7·4	
5	N(O·CH_2Ph)·COPh	Base	96	77—78	Aq. EtOH	$C_{25}H_{25}O_3N_2$	74·05	6·8	6·9		74·3	6·9	6·9	
5	N(OH)·COPh	Base	78 [k]	105—107	EtOH	$C_{18}H_{22}O_3N_2$	69·0	6·9	8·7		68·8	7·0	8·9	
5	N(COPh)·$[CH_2]_5$·O·C_6H_4·NH_2-*p*	2Me·SO_3H	82	137—139	EtOH–Et_2O	$C_{29}H_{37}O_5N_3S$, $2CH_4O_3S$			6·3	10·35			6·3	9·6
5	1,2-Dihydro-2-oxopyridyl	Base	96 [l]	114—115	EtOH	$C_{16}H_{20}O_2N_2$	70·3	7·5	10·2		70·6	7·35	10·3	
5	2-Oxopiperidino	Base	56 [m]	97—98	H_2O	$C_{16}H_{24}O_2N_2$	69·7	9·0	10·0		69·5	8·7	10·0	
5	2,3-Dihydro-3-oxobenzisothiazol-2-yl	Base	78 [n]	117—119	C_6H_6	$C_{18}H_{20}O_2N_2S$			8·5	10·1			8·5	9·8
5	2-Phthalimidoethoxy	Base	94	104—106	EtOH	$C_{21}H_{24}O_4N_2$	68·4	6·7	7·6		68·5	6·5	7·6	

TABLE 2. (*Continued.*)

n	R	Derivative	Yield (%)	M. p.	Recryst. from	Formula	Found (%) C	H	N	S	Required (%) C	H	N	S
2	4-Phthalimidobut-1-enyl	Base [a]		101—103	Aq. EtOH	$C_{20}H_{20}O_2N_2$	71·55	6·1	8·5		71·45	5·95	8·3	
5	NH·CO·NH [r]	Base	72	160—162	EtOH	$C_{23}H_{24}O_2N_4$	66·25	8·15	13·4		66·6	8·3	13·5	
5	NH·CO·CO·NH [r]	Base	79	150—152	2-Ethoxyethanol	$C_{24}H_{24}O_4N_2$	65·2	7·8	12·6		65·1	7·7	12·7	
5	*p*-NH·CO·C_6H_4·CO·NH [r]	Base	53	176—178	Xylene	$C_{30}H_{28}O_4N_4$	69·7	7·4	10·4		69·5	7·3	10·8	
5	NH·CO·$[CH_2]_3$·CO·NH [r]	Base	94	133—135 and 140—141	EtOH	$C_{27}H_{40}O_4N_4$	66·75	8·0	11·4		66·9	8·3	11·6	
		Me·SO_3H		227—230	EtOH	$C_{27}H_{40}O_4N_4,2CH_4O_3S$			8·2	9·6			8·3	9·45
8	NH·SO_2Ph	Base	79	121—122	EtOH	$C_{20}H_{20}O_3N_2S$			7·4	8·9			7·45	8·5
5	NH·SO_2·C_6H_4Me-*p*	Base	67	168—169	EtOH	$C_{18}H_{24}O_4N_2S,H_2O$ [p]			7·5	9·0			7·6	8·75
5	NH·SO_2·C_6H_4·NHAc-*p*	Base	79	117—119	Aq. MeOH	$C_{19}H_{23}O_4N_3S$			10·3				10·7	
		H_2SO_4		198—201		$2C_{19}H_{25}O_4N_3S,H_2SO_4$			9·25	11·3			9·5	10·95
5	NH·SO_2·C_6H_4·NH_2-*p*	Base	64 [q]	125—128	Aq. EtOH	$C_{17}H_{23}O_2N_3S$			11·6	9·1			12·0	9·2
		2Me·SO_3H		235—237		$C_{17}H_{23}O_2N_3S,2CH_4O_3S$			7·7	18·15			7·75	17·8
5	NPh·SO_2Me	Base	81	67—68	MeOH	$C_{18}H_{24}O_4N_2S$			7·9	9·1			8·0	9·2
5	NMe·SO_2Me	Base	81	76—77	EtOH–Et_2O	$C_{13}H_{22}O_4N_2S$			9·6	11·3			9·8	11·1
5	Tetrahydro-1,1-dioxo-1,2-thiazin-2-yl	Base	60	73	Et_2O	$C_{15}H_{24}O_3N_2S$	57·5	7·5	8·8		57·7	7·9	9·0	
5	1,1-Dioxonaphtho[1,8a,8-*cd*]-isothiazol-2-yl	Base	92	106—107	EtOH	$C_{21}H_{22}O_3N_2S$			7·3	8·35			7·3	8·4

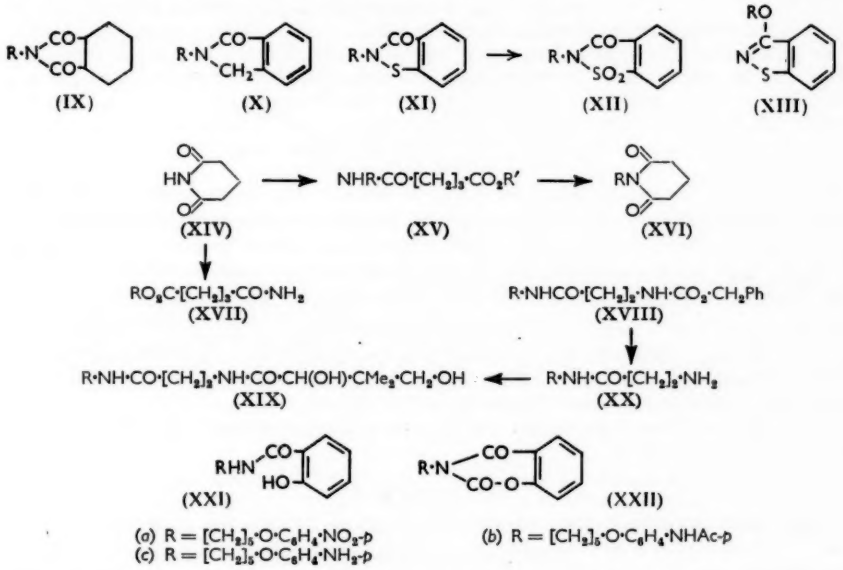
[a] Lit.,[19] m. p. 92—94°. [b] By acid hydrolysis of the *N*-acetyl derivative. [c] Overall from 1-amino-5-*p*-nitrophenoxypentane. [d] Found: Cl, 30·2. Required, Cl, 30·7%. [e] Pet = light petroleum. [f] Found: Cl, 17·7. Required, Cl, 17·9%. [g] Not obtained crystalline. Found: OEt, 5·8. Required OEt, 5·4%. [h] By alkaline hydrolysis of the corresponding methyl ester. [i] With decomp. [j] Overall from 1-anilino-5-*p*-nitrophenoxypentane. B. p. 215—220°/0·01 mm. [k] From 1-(*N*-benzyloxybenzamido)-5-*p*-nitrophenoxypentane. [l] By use of sodium sulphide. [m] From the preceding amine, or directly from 1-*p*-nitrophenoxy-5-(1,2-dihydro-2-oxopyridyl)pentane. [n] From the *N*-acetyl derivative, by refluxing for 48 hr. with N-hydrochloric acid (1 equiv.) in ethanol. [o] Methanesulphonate described in ref. 1. [p] Found: H_2O, 4·2. Required H_2O, 4·9%. [q] From the preceding acetyl derivative by hydrolysis with 2N-aqueous sodium hydroxide at 100°. [r] Bis-compound.

TABLE 3. *Miscellaneous compounds*, R·C_6H_4·O·$[CH_2]_5$·R′.

R	R′	M. p.	Recryst. from	Formula	Found (%) C	H	N	Required (%) C	H	N
p-NH·CHO	NHBz	163—164°	EtOH	$C_{19}H_{22}O_3N_2$			8·4			8·6
p-NHAc	NHBz	165—167	EtOH	$C_{20}H_{24}O_3N_2$			8·2			8·2
p-NHAc	NHAc	155—157	H_2O	$C_{15}H_{22}O_3N_2$	64·8	8·0	10·0	64·7	7·9	10·0
p-CO_2H·$[CH_2]_3$·CO·NH	$C_6H_4(CO)_2N$	185—187	AcOH	$C_{22}H_{24}O_6N_2$	65·3	6·0	6·6	65·1	5·7	6·6
p-NH_4O_2C·$[CH_2]_3$·CO·NH	$C_6H_4(CO)_2N$	174—176		$C_{22}H_{24}O_6N_2,NH_3,+1·5H_2O$	59·0	6·3	8·9	59·0	6·45	9·0
p-(5-Nitrofurfurylidene)amino ...	$C_6H_4(CO)_2N$	138—139	$CHCl_3$–EtOH	$C_{24}H_{21}O_6N_3$	64·6	5·0	9·4	64·6	4·7	9·4
p-Ph·CH=N	NHBz	133—134	EtOH	$C_{25}H_{26}O_3N_2$			7·3			7·25
p-MeN(NO)	$C_6H_4(CO)_2N$	104—105	EtOH	$C_{20}H_{21}O_4N_3$	65·65	5·9	11·2	65·4	5·8	11·4
o-NO_2	$C_6H_4(CO)_2N$	99·5	EtOH	$C_{19}H_{19}O_5N_3$			7·5			7·9
o-NH_2	$C_6H_4(CO)_2N$	94—95	EtOH	$C_{19}H_{20}O_3N_2$	70·4	6·2	8·6	70·4	6·2	8·6
m-NHAc	$C_6H_4(CO)_2N$	127·5—129	EtOH	$C_{21}H_{22}O_4N_2$			7·7			7·65
m-NH_2	$C_6H_4(CO)_2N$	102—103	EtOH	$C_{19}H_{20}O_3N_2$	70·35	6·2	8·7	70·4	6·2	8·6

preparation of this imide (XVIa) was attempted directly from 5-*p*-nitrophenoxypentyl bromide and glutarimide (XIV), the product was either the ethyl ester (XVa; R′ = Et) (when sodium ethoxide in ethanol was used for the condensation) or the 5-*p*-nitrophenoxypentyl ester (XVIIa) (when sodium hydroxide in aqueous ethanol was used).

Direct reaction of the amine (V; $n = 5$) with *p*-acetamidobenzoic acid to give the amide (VII; $n = 5$, R = *p*-C_6H_4·NHAc) was effected by using toluene-*p*-sulphonyl chloride in pyridine [7] or tetraethyl pyrophosphite in diethyl phosphite.[8] The latter method proved useful also in the synthesis of the pantothenamide (XIXc), providing the amide



(XVIIIa) from the starting nitro-amine (V; $n = 5$) and benzyloxycarbonyl-β-alanine in high yield. Removal of the protecting group with hydrogen bromide–acetic acid [9] and treatment of the β-alanylamide (XXa) with DL-pantolactone gave the nitro-pantothenamide (XIXa), which was reduced catalytically to the non-crystalline base (XIXc).

Attempts to reduce only the nitro-group of the cyanoacetamide (VII; $n = 5$; R = CH_2·CN) failed, but the amine (VIII; $n = 5$; R = CH_2·CN) was formed in high yield by preferential reaction of ethyl cyanoacetate with the aliphatic amino-group of 1-amino-5-*p*-aminophenoxypentane (VI; $n = 5$). Other reactive esters such as methyl dichloroacetate and trichloroacetate behaved similarly. Special methods employed for individual compounds included the reaction of the nitro-amine (V; $n = 5$) with 2-phenyloxazolone to form the hippuramide (VII; $n = 5$; R = CH_2·NH·COPh), and successively with methyl salicylate and with ethyl chloroformate to give first the salicylylamide (XXIa) and then the 3,4-dihydro-2,4-dioxo-5,6-benz-1,3-oxazine (XXIIa). Catalytic reduction then gave the required amines (XXIc) and (XXIIc).

Since both the 5-phenylpentyl ether [1] and the 5-phthalimidopentyl ether of *p*-aminophenol were active schistosomicides, the preparation of the 5-phenyl-5-phthalimidopentyl ether (XXVIb) was undertaken. 4-Benzoylbutyl bromide [10] was converted into the *p*-nitrophenyl ether (XXIIIa) which was reduced by the Meerwein–Ponndorf method to

[7] Brewster and Ciotti, *J. Amer. Chem. Soc.*, 1955, **77**, 6214.
[8] Anderson, Blodinger, and Welcher, *ibid.*, 1952, **74**, 5309.
[9] Ben-Ishai, *J. Org. Chem.*, 1954, **19**, 62.
[10] Perkin, *J.*, 1887, 731.

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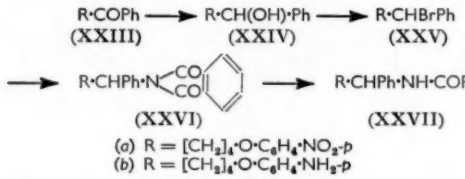
the alcohol (XXIVa). The bromide (XXVa), formed by means of phosphorus tribromide, was treated with potassium phthalimide, yielding the nitro-imide (XXVIa) which was reduced catalytically to the base (XXVIb). Treating the phthalimide (XXVIa) with hydrazine gave the free nitro-amine which was successively benzoylated and reduced to the analogous 5-benzamido-5-phenyl ether (XXVIIb).

Condensation of *p*-*N*-methylacetamidophenol with 5-phthalimidopentyl bromide and subsequent hydrolysis of the acetyl group led to the *N*-methyl derivative of the amino-imide (IV; $n = 5$). This compound was remarkable for its scarlet colour in the solid



(*a*) R = $[CH_2]_4$·O·C_6H_4·NO_2-*p*
(*b*) R = $[CH_2]_4$·O·C_6H_4·NH_2-*p*

state, although its dilute solutions were colourless. The corresponding *NN*-dimethyl derivative was only pale yellow. The colour of the primary amines of this series had already been noted by Belotsvetov,[11] who recorded the orange-yellow colour of both 1-*p*-aminophenoxy- and 1-*p*-dimethylaminophenoxy-3-phthalimidopropane. *N*-Acetyl-1-*p*-methylaminophenoxy-5-phthalimidopentane with hydrazine gave the 5-amino-derivative which was benzoylated and hydrolysed to 5-benzamido-1-*p*-methylaminophenoxypentane: use of the *N*-formyl compound was less satisfactory. An attempt to prepare this amine by partial benzoylation of 5-amino-1-*p*-methylaminophenoxypentane was unsuccessful, giving a mixture of dibenzoyl derivative and unchanged amine.

Several miscellaneous secondary and tertiary amines of a similar type are described in the Experimental section.

Experimental

Light petroleum refers, unless otherwise stated, to the fraction of b. p. 40—60°.

Nitro- and acylamido-compounds.

1-p-*Nitrophenoxy*-2-*phthalimidoethane* was prepared (22%) from potassium *p*-nitrophenoxide and 2-phthalimidoethyl bromide by the method already described.[1] After crystallisation from acetic acid, it had m. p. 152—154° (Found: N, 9·2. $C_{16}H_{12}O_5N_2$ requires N, 9·0%). Similarly prepared in either ethanol or 2-ethoxyethanol were: 1-p-*nitrophenoxy*-3-*phthalimidopropane* (44%), m. p. 189—191·5° (from dioxan) (Found: N, 8·75. $C_{17}H_{14}O_5N_2$ requires N, 8·6%); 1-p-*nitrophenoxy*-4-*phthalimidobutane* (64%), m. p. 119° (from acetic acid) (Found: C, 63·8; H, 4·7; N, 8·5. $C_{18}H_{16}O_5N_2$ requires C, 63·5; H, 4·7; N, 8·2%); 1-p-*nitrophenoxy*-10-*phthalimidodecane* (60%), m. p. 102—103° (from acetic acid) (Found: C, 67·8; H, 7·0; N, 6·6. $C_{24}H_{28}O_5N_2$ requires C, 67·8; H, 6·6; N, 6·6%); and 1-p-*nitrophenoxy*-6-*phthalimidohex*-3-*ene* (55%) (from 6-phthalimido-1-toluene-*p*-sulphonyloxyhex-3-ene; B. P. 769,706), m. p. 118—119° (from aqueous acetic acid) (Found: C, 65·7; H, 5·2; N, 7·5. $C_{20}H_{18}O_5N_2$ requires C, 65·6; H, 4·9; N, 7·65%).

1-*Amino*-5-p-*nitrophenoxypentane*.—1-*p*-Nitrophenoxy-5-phthalimidopentane was treated with aqueous hydrazine in ethanol as already described,[1] but the amine was more conveniently liberated by shaking the resulting complex with chloroform and warm 2N-sodium hydroxide. The *amine* had b. p. 160—165°/0·02 mm. (partial decomp.) (Found: N, 12·9. $C_{11}H_{16}O_3N_2$ requires N, 12·5%). Similarly prepared were: 1-*amino*-5-p-*aminophenoxypentane* (94%), m. p. 67—69° [from light petroleum (b. p. 100—120°)] (Found: N, 14·1. $C_{11}H_{18}ON_2$ requires N, 14·4%) [*dimethanesulphonate*, m. p. 244—246° (from ethanol) (Found: N, 7·4; S, 16·8. $C_{11}H_{18}ON_2,2CH_4O_3S$ requires N, 7·25; S, 16·6%)]; and 1-p-*acetamidophenoxy*-5-*aminopentane* (91%), m. p. 137—139° (from benzene) (Found: C, 65·7; H, 8·45; N, 11·9. $C_{13}H_{20}O_2N_2$ requires C, 66·1; H, 8·5; N, 11·85%) [*methanesulphonate*, m. p. 155—157° (from ethanol) (Found: N, 8·4. $C_{13}H_{20}O_2N_2,CH_4O_3S$ requires N, 8·4%)].

[11] Belotsvetov, *J. Gen. Chem. U.S.S.R.*, 1944, **14**, 226.

1-p-*Nitrophenoxy*-5-*tetrachlorophthalimidopentane*.—A mixture of 5-amino-1-*p*-nitrophenoxypentane (22·4 g.) and tetrachlorophthalic anhydride (28·6 g.) was heated at 180—190° for 2 hr., cooled somewhat, and dissolved in hot 2-ethoxyethanol (150 ml.). The cooled solution deposited the *tetrachlorophthalimide* (96%), m. p. 165—167° (Found: N, 5·7; Cl, 28·5. $C_{19}H_{14}O_5N_2Cl_4$ requires N, 5·7; Cl, 28·8%). Similarly prepared were: 1-p-*nitrophenoxy*-5-3′-*nitrophthalimidopentane* (84%), m. p. 163—164·5° (from 2-ethoxyethanol) (Found: N, 10·45. $C_{19}H_{17}O_7N_3$ requires N, 10·5%); 1-p-*acetamidophenoxy*-5-3′-*nitrophthalimidopentane* (67%), m. p. 132—134° (from ethanol) (Found: N, 10·2. $C_{21}H_{21}O_6N_3$ requires N, 10·3%); and 1-*homophthalimido*-5-p-*nitrophenoxypentane* (65%), m. p. 144—145° (from acetone) (Found: C, 65·2; H, 5·6; N, 7·5. $C_{20}H_{20}O_5N_2$ requires C, 65·2; H, 5·4; N, 7·6%).

1-(5-p-*Nitrophenoxypentyl*)*barbituric Acid*.—A mixture of 1-*p*-nitrophenoxy-5-ureidopentane[1] (61 g.), malonic acid (24 g.), and acetic acid (55 ml.) was heated to 70—80° and treated dropwise with acetic anhydride (45 ml.). After a further 8 hr. at 90°, the mixture was cooled, diluted with water (84 ml.), and filtered from some solid [m. p. 178·5—180° (from acetone), which was possibly an acetyl derivative (Found: C, 54·0; H, 5·3; N, 11·1. Calc. for $C_{17}H_{19}O_7N_3$: C, 54·1; H, 5·0; N, 11·1%)]. Further dilution with water (240 ml.) gave the substituted *barbituric acid*, m. p. 149—151° (from ethanol) (Found: C, 53·85; H, 5·1; N, 12·5. $C_{15}H_{17}O_6N_3$ requires C, 53·7; H, 5·1; N, 12·5%).

1-p-*Nitrophenoxy*-5-*salicylylamidopentane*.—A mixture of 5-amino-1-*p*-nitrophenoxypentane (45 g.) and methyl salicylate (15·2 g.) was heated at 120° for 5 hr., cooled, and dissolved in chloroform. The solution was washed with 2N-hydrochloric acid and water, dried, and evaporated. The residue was crystallised from benzene, yielding the *amide* (73%), m. p. 123—125° (Found: N, 8·2. $C_{18}H_{20}O_5N_2$ requires N, 8·15%).

3,4-*Dihydro*-3-(5-p-*nitrophenoxypentyl*)-2,4-*dioxo*-5,6-*benz*-1,2-*oxazine*.—Ethyl chloroformate (12 g.) was slowly added to a cooled solution of the foregoing nitro-compound (35 g.) in dry pyridine (120 ml.). The mixture was heated at 100° for 2 hr., cooled, and diluted with water, and the product was crystallised from acetic acid and from ethanol, giving the *benzoxazinedione* (86%), m. p. 145—146° (Found: C, 61·8; H, 5·1; N, 7·5. $C_{19}H_{18}O_6N_2$ requires C, 61·6; H, 4·9; N, 7·6%).

1-*Camphorimido*-5-p-*nitrophenoxypentane*.—A mixture of 5-*p*-nitrophenoxypentyl bromide (16·15 g.), (±)-camphorimide (10·15 g.), 10·4N-potassium hydroxide (5·4 ml.), and 2-ethoxyethanol (25 ml.) was refluxed for 2 hr., cooled, and diluted with water. The solid was recrystallised from aqueous ethanol, giving the *camphorimide* (71%), m. p. 66—67° (Found: C, 64·9; H, 7·5; N, 7·4. $C_{21}H_{28}O_5N_2$ requires C, 64·9; H, 7·3; N, 7·2%). N-(5-p-*Nitrophenoxypentyl*)*phthalhydrazide* (23%), m. p. 160—162° (from toluene) (Found: C, 61·95; H, 5·35; N, 11·7. $C_{19}H_{19}O_5N_5$ requires C, 61·8; H, 5·2; N, 11·4%), was similarly made (in dimethylformamide).

1-β-*Carboxyacrylamido*-5-p-*nitrophenoxypentane*.—A solution of 1-amino-5-*p*-nitrophenoxypentane (22·4 g.) in chloroform (100 ml.) was slowly added to a suspension of maleic anhydride (9·8 g.) in chloroform (100 ml.). When the exothermic reaction was over, the solution was refluxed for 1 hr., cooled, washed with 2N-hydrochloric acid and water, dried, and evaporated. Crystallisation of the residue from ethanol gave the *maleamic acid* (53%), m. p. 91—93° (Found: C, 55·6; H, 5·8; N, 8·3. $C_{15}H_{18}O_6N_2$ requires C, 55·9; H, 5·6; N, 8·7%). Similarly prepared were: 1-p-*acetamidophenoxy*-5-β-*carboxyacrylamidopentane* (63%), m. p. 161—163° (from aqueous acetic acid) (Found: C, 60·4; H, 6·8; N, 8·7. $C_{17}H_{22}O_5N_2$ requires C, 61·1; H, 6·6; N, 8·4%); 1-(β-carboxymethyl-β-methylvaleramido)-5-*p*-nitrophenoxypentane (not obtained crystalline); and 1-*γ-carboxybutyramido*-5-p-*nitrophenoxypentane* (92%), m. p. 116—117° (also obtained by hydrolysis of the corresponding ethyl ester as described below).

1-*Maleimido*-5-p-*nitrophenoxypentane*.—A mixture of the foregoing maleamic acid (17·2 g.), acetic anhydride (18 ml.), and freshly fused sodium acetate (1·8 g.) was stirred at 100° for 1 hr., and excess of the anhydride was removed *in vacuo*. The residue was triturated with water, and the solid product crystallised from aqueous ethanol and from light petroleum (b. p. 100—120°), giving the *maleimide* (51%), m. p. 105—107° (Found: C, 59·1; H, 5·1; N, 9·2. $C_{15}H_{16}O_5N_2$ requires C, 59·2; H, 5·3; N, 9·2%).

1-*Glutarimido*-5-p-*nitrophenoxypentane*.—A mixture of the glutaramic acid (37·3 g.) and acetyl chloride (100 ml.) was refluxed for 20 min., then evaporated, and the residue was crystallised from methanol, yielding the *glutarimide* (84%), m. p. 87—88° (Found: C, 59·7; H, 6·2; N, 8·9. $C_{16}H_{20}O_5N_2$ requires C, 60·0; H, 6·3; N, 8·75%). 1-(β-Ethyl-β-methylglutarimido)-5-*p*-nitrophenoxypentane was made similarly, but was not obtained crystalline.

1-*γ-Ethoxycarbonylbutyramido*-5-p-*nitrophenoxypentane*.—Glutarimide (11·3 g.) and 5-*p*-nitrophenoxypentyl bromide (28·8 g.) were added to a solution of sodium (2·3 g.) in ethanol (150 ml.), and the mixture was refluxed for 20 hr., cooled, diluted with water, and extracted with chloroform. The washed and dried extract was evaporated and the residue was crystallised from benzene, giving the *ethyl ester* (39%), m. p. 90—91·5° (Found: C, 59·0; H, 7·3; N, 7·3; OEt, 12·3%; *M*, 300. $C_{18}H_{26}O_6N_2$ requires C, 59·0; H, 7·15; N, 7·6; OEt, 12·3%; *M*, 366). Hydrolysis with 2N-sodium hydroxide (1 equiv.) afforded the corresponding *acid* (93%), m. p. 118—119° (Found: C, 56·9; H, 6·8; N, 8·3. $C_{16}H_{22}O_6N_2$ requires C, 56·8; H, 6·6; N, 8·3%) not depressed by a specimen prepared as described above.

When a similar condensation was carried out by using sodium hydroxide (1 equiv.) in aqueous ethanol, the product (33%) was 5-p-*nitrophenoxypentyl glutaramate*, m. p. 93—95° (from benzene) (Found: C, 56·9; H, 6·3; N, 8·3%; *M*, 330. $C_{16}H_{22}O_6N_2$ requires C, 56·8; H, 6·6; N, 8·3%; *M*, 338), identical with a specimen, m. p. 93—94°, prepared (34%) from 5-*p*-nitrophenoxypentyl bromide and silver glutaramate in dry dioxan. Its structure was confirmed by catalytic reduction to 5-p-*aminophenoxypentyl glutaramate* (81%), m. p. 116—118° (from ethanol) (Found: N, 9·0. $C_{16}H_{24}O_4N_2$ requires N, 9·1%), and subsequent hydrolysis to 5-*p*-aminophenoxypentanol, m. p. 94—96° (Found: N, 7·2. Calc. for $C_{11}H_{17}O_2N$: N, 7·2%) not depressed by an authentic specimen (see Part II).

The amides (listed in Table 1) were prepared from 1-*p*-acetamidophenoxy-5-aminopentane, 1-amino-4-*p*-nitrophenoxybutane, 1-amino-5-*p*-nitrophenoxypentane or 1-amino-8-*p*-nitrophenoxyoctane with the appropriate acid chloride or anhydride either in pyridine or under Schotten–Baumann conditions (in some instances the yields quoted are overall from the phthalimide). NN′-*Di*-(5-p-*nitrophenoxypentyl*)*terephthalamide* (58%), m. p. 154—157° (from ethanol) (Found: N, 9·7. $C_{30}H_{34}O_8N_4$ requires N, 9·6%), and NN′-*Di*-(5-p-*nitrophenoxypentyl*)*glutaramide* (39%), m. p. 127—129° (from acetone) (Found: N, 10·4. $C_{27}H_{36}O_8N_4$ requires N, 10·3%), were prepared similarly.

1-*Cyanoacetamido*-5-p-*nitrophenoxypentane* was prepared (68%) from 1-amino-5-*p*-nitrophenoxypentane and ethyl cyanoacetate in boiling ethanol. After recrystallisation from aqueous ethanol, it had m. p. 85—86° (Found: C, 57·55; H, 5·8; N, 14·3. $C_{14}H_{17}O_4N_3$ requires C, 57·75; H, 5·9; N, 14·4%). Similarly obtained (in the absence of a solvent) was NN′-*di*-(5-p-*nitrophenoxypentyl*)*oxamide* (73%), m. p. 163·5—164·5° (from chloroform–ethanol) (Found: C, 57·25; H, 5·8; N, 11·2. $C_{24}H_{30}O_8N_4$ requires C, 57·4; H, 6·0; N, 11·1%).

1-*Ethoxalylamino*-5-p-*nitrophenoxypentane*.—Ethoxalyl chloride (13·65 g.) was slowly added to a cooled solution of 1-amino-5-*p*-nitrophenoxypentane (21·4 g.) in pyridine (100 ml.). The solution was kept overnight at room temperature, diluted with water and ether, and filtered from the insoluble oxamide (2·15 g.). The ether solution was separated, washed with 2N-hydrochloric acid and water, dried, and evaporated. The residue was repeatedly extracted with boiling light petroleum (b. p. 100—120°). The cooled extracts deposited the *ethoxalyl derivative* (27%), m. p. 85—87° (Found: C, 55·9; H, 5·95; N, 8·8. $C_{15}H_{20}O_6N_2$ requires C, 55·55; H, 6·2; N, 8·6%).

1-*Formamido*-5-p-*nitrophenoxypentane*.—A mixture of 1-*amino*-5-p-*nitrophenoxypentane* (36·4 g.), concentrated hydrochloric acid (13·95 ml.), and formamide (64·5 ml.) was heated at 145° for 30 min., cooled, and evaporated under reduced pressure. Water (100 ml.) was added to the residue, and the solid product was filtered off, dried, and recrystallised from benzene. The crude nitro-compound was extracted with ether (Soxhlet), and the extract was cooled and filtered, giving the *formamide* (78%), m. p. 71—72° (Found: C, 57·25; H, 6·4; N, 11·3. $C_{12}H_{16}O_4N_2$ requires C, 57·15; H, 6·35; H, 11·1%).

1-*Hippuramido*-5-p-*nitrophenoxypentane*.—2-Phenyloxazolone (8·6 g.) was added to a solution of 1-amino-5-*p*-nitrophenoxypentane (12·0 g.) in chloroform, the solution was evaporated, and the residue was heated at 100° for 30 min. Crystallisation of the residue from ethanol gave the *hippuramide* (80%), m. p. 145—147° (Found: N, 10·7. $C_{20}H_{23}O_5N_3$ requires N, 10·9%).

1-o-*Carboxybenzamido*-5-p-*nitrophenoxypentane*.—1-*p*-Nitrophenoxy-5-phthalimidopentane (17·7 g.) was refluxed with N-sodium hydroxide (50 ml.) for 15 min. The yellow solution was filtered and the filtrate was acidified with acetic acid. The *acid* was filtered off, washed with dilute acetic acid and water, dried, and recrystallised from chloroform–light petroleum. Its m. p., 118—122°, varied with the rate of heating (Found: C, 61·4; H, 5·5; N, 7·4. $C_{19}H_{20}O_6N_2$ requires C, 61·3; H, 5·4; N, 7·5%).

1-p-*Acetamidobenzamido*-5-p-*nitrophenoxypentane*.—(*a*) Tetraethyl pyrophosphite (2·7 ml.)

was added to a solution of 1-amino-5-*p*-nitrophenoxypentane (2·24 g.) and *p*-acetamidobenzoic acid (1·79 g.) in diethyl phosphite (7 ml.), and the mixture was heated at 100° for 1 hr., diluted with water, and cooled. Recrystallisation of the product from 2-ethoxyethanol gave the *amide* (55%), m. p. 187—188° (Found: N, 10·95. $C_{20}H_{23}O_5N_3$ requires N, 10·9%).

(*b*) 1-Amino-5-*p*-nitrophenoxypentane (11·2 g.) was added to a solution of *p*-acetamidobenzoic acid (17·9 g.) and toluene-*p*-sulphonyl chloride (9·52 g.) in pyridine (40 ml.). After 30 min. at room temperature, the mixture was treated with a solution of sodium hydroxide (10 g.) and sodium metabisulphite (5 g.) in water (200 ml.), and the precipitate was filtered off, washed, dried, and recrystallised. The amide (60%) had m. p. 185—186°.

1-*Dibenzoylamino*-5-p-*nitrophenoxypentane*.—A solution of 1-amino-5-*p*-nitrophenoxypentane (2·54 g.) in pyridine (10 ml.) was refluxed with benzoyl chloride (5 ml.) for 1·5 hr., cooled, and diluted with water. After recrystallisation from ethanol, the *dibenzoyl derivative* (83%) had m. p. 119—120° (Found: N, 6·8. $C_{25}H_{24}O_5N_2$ requires N, 6·5%).

1-(N-*Benzyloxycarbonyl*-β-*alanyl*)*amino*-5-p-*nitrophenoxypentane*.—A solution of benzyloxycarbonyl-β-alanine [12] (24 g.) and 1-amino-5-*p*-nitrophenoxypentane (24 g.) in diethyl phosphite (75 ml.) was heated with tetraethyl pyrophosphite (30 ml.) at 100° for 30 min., diluted with water, cooled, and filtered. The product was recrystallised from aqueous ethanol; the *benzyloxycarbonyl compound* (90%) had m. p. 137—138° (Found: N, 9·65. $C_{22}H_{27}O_6N_3$ requires N, 9·8%).

1-β-*Alanylamino*-5-p-*nitrophenoxypentane*.—33% Hydrogen bromide–acetic acid (60 ml.) was added to the foregoing benzyloxycarbonyl derivative (35·05 g.) in a flask fitted with a guard tube ($CaCl_2$). Evolution of carbon dioxide began at once. After 20 min. the clear solution was treated with dry ether, and the hydroscopic hydrobromide was filtered off, washed with dry ether, and dissolved in water. The solution was basified and extracted with chloroform, the washed and dried extract was evaporated, and the residue was triturated with ether. The solid product (m. p. 85—92°) proved difficult to purify and was used directly for the next stage. A small amount was recrystallised from benzene, giving the β-*alanyl compound*, m. p. 93—95° (Found: C, 57·6; H, 7·2; N, 13·6. $C_{14}H_{21}O_4N_3$ requires C, 56·9; H, 7·2; N, 14·2%).

1-p-*Nitrophenoxy*-5-DL-*pantothenamidopentane*.—A solution of the foregoing amine (10·36 g.) and DL-pantolactone [13] (4·56 g.) in absolute ethanol (50 ml.) was refluxed for 20 hr., then evaporated. The residue, in ethyl acetate, was washed with 2N-sodium hydroxide, 2N-hydrochloric acid, and water, dried, and evaporated, and the residual oily *product* (14·6 g.) (Found: N, 9·2. $C_{20}H_{31}O_7N_3$ requires N, 9·9%) was reduced directly to the amine.

1-*Cyclohexylamino*-5-p-*nitrophenoxypentane*.—A solution of 5-*p*-nitrophenoxypentyl bromide (43·2 g.) and cyclohexylamine (19·8 g.) in ethanol (50 ml.) was refluxed for 19 hr., cooled, and filtered. The *amine hydrobromide* (76%), after recrystallisation from ethanol, had m. p. 221—223° (Found: C, 53·1; H, 7·2; N, 7·35. $C_{17}H_{26}O_3N_2$,HBr requires C, 52·7; H, 7·0; N, 7·2%). The *benzoyl derivative* had m. p. 78—79° (from aqueous ethanol) (Found: N, 7·0. $C_{24}H_{30}O_4N_2$ requires N, 6·8%).

1-N-*Benzyloxybenzamido*-5-p-*nitrophenoxypentane*.—5-*p*-Nitrophenoxypentyl bromide (44·5 g.) and *N*-benzyloxybenzamide [14] (35 g.) were added to a solution from sodium (3·5 g.) and dry ethanol (300 ml.), and the mixture was refluxed for 24 hr., filtered from sodium bromide, and concentrated. The residue was dissolved in chloroform, and the solution was washed with 2N-sodium hydroxide and water, dried, concentrated, and diluted with ether, giving the *nitroether* (46%), m. p. 77—78° (Found: C, 69·1; H, 6·1; N, 6·4. $C_{25}H_{26}O_5N_2$ requires C, 69·1; H, 6·0; N, 6·45%).

1-*Anilino*-5-p-*nitrophenoxypentane*.—A mixture of 5-*p*-nitrophenoxypentyl bromide (57·6 g.), aniline (50 ml.), and ethanol (200 ml.) was refluxed for 20 hr., concentrated, and diluted with water. Crystallisation of the product from ethanol gave the *anilino-derivative* (98%), m. p. 87—89° (Found: C, 67·7; H, 6·4; N, 9·1. $C_{17}H_{20}O_3N_2$ requires C, 68·0; H, 6·7; N, 9·3%). The acetyl derivative was not obtained crystalline and was reduced directly to the amine (see Table 2). The *methanesulphonyl derivative* (64%) had m. p. 73—74° [from benzene–light petroleum (b. p. 80—100°)] (Found: N, 7·0; S, 8·3. $C_{18}H_{22}O_5N_2S$ requires N, 7·4; S, 8·5%).

1-N-*Methylmethanesulphonamido*-5-p-*nitrophenoxypentane*.—1-Methanesulphonamido-5-*p*-nitrophenoxypentane (42·7 g.), water (5 ml.), and methyl iodide (17·4 ml.) were added successively to a solution from sodium (3·5 g.) and ethanol (300 ml.). The mixture was refluxed for 3 hr.,

[12] Sifferd and du Vigneaud, *J. Biol. Chem.*, 1935, **108**, 753.
[13] Stiller, Harris, Finkelstein, Keresztesy, and Folkers, *J. Amer. Chem. Soc.*, 1940, **62**, 1785.
[14] Beckman, *Ber.*, 1893, **26**, 2631.

concentrated, and diluted with water, and the solid product was crystallised from ether, giving the N-*methylmethanesulphonamide* (78%), m. p. 61—63° (Found: N, 8·6; S, 9·9. $C_{13}H_{20}O_5N_2S$ requires N, 8·9; S, 10·1%).

N-*Benzoyldi*-(4-p-*nitrophenoxypentyl*)*amine*.—A solution of 5-*p*-nitrophenoxypentyl bromide (28·8 g.) and 1-amino-5-*p*-nitrophenoxypentane (22·4 g.) in ethanol (250 ml.) was refluxed for 20 hr., cooled, and filtered. The crude hydrobromide (68%) was shaken with benzoyl chloride in acetone–2N-sodium hydroxide, and the product was crystallised from acetone–ether, giving the *benzoyl derivative* (66%), m. p. 114—115·5° (Found: C, 65·1; H, 6·3; N, 7·8. $C_{29}H_{33}O_7N_3$ requires C, 65·05; H, 6·2; N, 7·8%).

1-*Benzoyl*-4-p-*nitrophenoxybutane* was obtained (89%) by condensation of potassium *p*-nitrophenoxide with 4-benzoylbutyl bromide [10] in 2-ethoxyethanol; after crystallisation from acetic acid, it had m. p. 122—123° (Found: C, 68·3; H, 6·0; N, 4·7. $C_{17}H_{17}O_4N$ requires C, 68·2; H, 5·7; N, 4·7%).

1-*Hydroxy*-5-p-*nitrophenoxy*-1-*phenylpentane*.—A solution of the foregoing nitro-ketone (63 g.) and aluminium isopropoxide (25·2 g.) in propan-2-ol (3 l.) was slowly distilled until no more acetone was obtained (2 hr.). The solution was evaporated, the residue was treated with dilute hydrochloric acid, and the solid was recrystallised from aqueous ethanol, giving the *hydroxy-compound* (94%), m. p. 61—62° (Found: C, 67·7; H, 6·2; N, 4·75. $C_{17}H_{19}O_4N$ requires C, 67·8; H, 6·3; N, 4·65%).

5-p-*Nitrophenoxy*-1-*phenyl*-1-*phthalimidopentane*.—Phosphorus tribromide (21·6 ml.) was slowly added to a solution of the foregoing hydroxy-compound (54 g.) in benzene (500 ml.), stirred and cooled to 10°; the mixture was then kept overnight at room temperature and treated with water, the benzene layer was separated, and the aqueous layer was extracted with ether. The combined benzene and ether solutions were washed, dried, and evaporated. A mixture of the residual bromo-compound, potassium phthalimide (54 g.), and dry acetone (250 ml.) was stirred and refluxed for 48 hr. The product (34 g.) was isolated in the usual way. Unchanged bromide recovered from the mother-liquors was re-treated with potassium phthalimide in acetone, giving more of the required product (total 51 g., 66%). After recrystallisation from ethanol, the *phthalimido-derivative* had m. p. 131—132° (Found: C, 69·8; H, 4·7; N, 6·6. $C_{25}H_{22}O_5N_2$ requires C, 69·8; H, 5·1; N, 6·5%). Hydrolysis with hydrazine and subsequent benzoylation afforded 1-*benzamido*-5-p-*nitrophenoxy*-1-*phenylpentane* (69% overall), m. p. 116—118° (from benzene) (Found: C, 71·6; H, 5·9. $C_{24}H_{24}O_4N_2$ requires C, 71·8; H, 5·9%).

1-p-*Nitrophenoxy*-5-2′-*phthalimidoethoxypentane*.—1-2′-Hydroxyethoxy-5-*p*-nitrophenoxypentane [15] was converted by toluene-*p*-sulphonyl chloride in pyridine into the *toluene*-p-*sulphonyl derivative* (81%), m. p. 49—50° (Found: C, 56·95; H, 5·8; N, 3·4. $C_{20}H_{25}O_7NS$ requires C, 56·7; H, 5·9; N, 3·3%), which was condensed with potassium phthalimide in the usual way, giving the *phthalimido-derivative* (65%), m. p. 78—79° (from methanol) (Found: C, 63·5; H, 5·9; N, 6·9. $C_{21}H_{22}O_6N_2$ requires C, 63·3; H, 5·5; N, 7·0%).

1-(1,2-*Dihydro*-2-*oxo*-*pyrid*-1-*yl*)-5-p-*nitrophenoxypentane*.—A mixture of 5-*p*-nitrophenoxypentyl iodide (Part II) (102 g.), the sodium derivative (36 g.) of 2-pyridone, ethanol (400 ml.), and water (200 ml.) was refluxed for 24 hr., ethanol was distilled off, and the residue was diluted with water. The solid product was recrystallised from acetone, giving the *nitro-ether* (47%), m. p. 103° (Found: C, 63·7; H, 6·2; N, 9·1. $C_{16}H_{18}O_4N_2$ requires C, 63·6; H, 6·0; N, 9·3%). From the mother-liquors a small amount of 1-*p*-nitrophenoxy-5-pyrid-2′-yloxypentane (Part II) was obtained.

1-(2,3-*Dihydro*-3-*oxobenzisothiazol*-2-*yl*)-5-p-*nitrophenoxypentane*.—A mixture of 5-*p*-nitrophenoxypentyl bromide (2·88 g.), the sodium derivative (1·73 g.) of 2,3-dihydro-3-oxobenzisothiazole,[16] and 2-ethoxyethanol (10 ml.) was refluxed for 20 hr., cooled, and diluted with water. The solid product was dissolved in chloroform, the solution was washed with dilute sodium hydroxide and water, dried, and evaporated, and the residue was triturated with ether. Recrystallisation of the solid from ethanol yielded the *nitro-ether* (39%), m. p. 109—111° (Found: N, 7·5; S, 9·0. $C_{18}H_{18}O_4N_2S$ requires N, 7·8; S, 8·9%). Oxidation with 30% hydrogen peroxide in acetic acid at 100° gave the known saccharin derivative,[1] m. p. and mixed m. p. 126—127°.

1-p-*Acetamidophenoxy*-5-(2,3-*dihydro*-3-*oxobenzisothiazol*-2-*yl*)*pentane* (42%), m. p. 170—171° (from ethanol) (Found: C, 61·7; H, 6·6; N, 7·05; S, 8·4. $C_{20}H_{22}O_4N_2S$ requires C, 62·1;

[15] May and Baker Ltd., B.P. 770,870.
[16] McClelland and Gait, *J.*, 1926, 923.

H, 5·7; N, 7·25; S, 8·3%) was similarly prepared. When 5-*p*-nitrophenoxypentyl bromide (3·15 g.) was condensed with 2,3-dihydro-3-oxobenzisothiazole (1·65 g.) by using potassium carbonate (0·76 g.) in acetone (50 ml.), the product (1·9 g.) had m. p. 97—99° (from acetic acid) (Found: C, 59·7; H, 5·0; N, 7·5; S, 9·0%; *M*, 350. $C_{18}H_{18}O_4N_2S$ requires C, 60·3; H, 5·1; N, 7·8; S, 8·9%; *M*, 358), depressed to below 90° by the foregoing nitro-compound, and was probably 1-p-*nitrophenoxy-5-benzisothiazol-3′-yloxypentane*.

3-(5-p-*Nitrophenoxypentyl*)*rhodanine*.—Carbon disulphide (8·4 ml.) and dimethylformamide (60 ml.) were added successively to a solution of 5-amino-1-*p*-nitrophenoxypentane (32 g.) in dry toluene (100 ml.). After 30 min. the solution was cooled, treated with mercuric oxide (32 g.), and shaken for 30 min., then filtered from black mercuric sulphide, and the filtrate was treated with 90% mercaptoacetic acid (7·3 g.). The solution was heated at 100° for 30 min., concentrated, and diluted with water, and the solid product was recrystallised from ethanol, giving the *rhodanine* (68%), m. p. 112—113° (Found: C, 49·6; H, 5·1; S, 18·8. $C_{14}H_{16}O_4N_2S_2$ requires C, 49·4; H, 4·7; S, 18·8%). The 5-*benzylidene-derivative*, prepared (96%) by heating the rhodanine (30 g.) with benzaldehyde (20 ml.), acetic acid (200 ml.), and concentrated sulphuric acid (40 ml.) at 100° for 3 hr., crystallised from acetic acid and had m. p. 143—144° (Found: N, 6·4; S, 14·9. $C_{21}H_{20}O_4N_2S_2$ requires N, 6·5; S, 14·95%).

3-(5-p-*Nitrophenoxypentyl*)*thiazolidine*-2,4-*dione*.—Thiazolidine-2,4-dione (14·1 g.) and 5-*p*-nitrophenoxypentyl iodide (49·7 g.) were added successively to a solution from sodium (3·43 g.) and dry ethanol (200 ml.), and the mixture was refluxed for 20 hr., cooled, and filtered. The solid was washed with cold ethanol and water, and recrystallised from ethanol, giving the *thiazolidine*-2,4-*dione* (46%), m. p. 118—119° (Found N, 8·55; S, 9·7. $C_{14}H_{16}O_5N_2S$ requires N, 8·6; S, 9·8%).

N-(5-p-*Nitrophenoxypentyl*)*butane*-1,4-*sultam*—Butane-1,4-sultam[17] (2 g.) was dissolved in a solution from sodium (0·35 g.) and dry ethanol (10 ml.), and a solution from 5-*p*-nitrophenoxypentyl bromide (4·3 g.) in dry ethanol (10 ml.) was added. The mixture was refluxed for 3 hr., concentrated, diluted with water, and filtered. Recrystallisation of the solid from methanol yielded the *sultam* (79%), m. p. 89—90° (Found: C, 53·0; H, 6·5; N, 8·2; S, 9·0. $C_{15}H_{22}O_5N_2S$ requires C, 52·6; H, 6·4; N, 8·2; S, 9·35%). N-(5-p-*Nitrophenoxypentyl*)*naphthalene*-1,8-*sultam* (59%), m. p. 119° (from ethanol) (Found: N, 6·9; S, 8·0. $C_{21}H_{22}O_5N_2S$ requires N, 6·8; S, 7·8%), was similarly prepared from naphthalene-1,8-sultam.[18]

Primary amines.

1-p-*Aminophenoxy*-7-*hexahydrophthalimidoheptane*.—When 1-*p*-nitrophenoxy-7-phthalimidoheptane (43·8 g.) was reduced in ethanol (350 ml.) over 2% platinum dioxide at 70° and 56 lb. per sq. inch hydrogen pressure, the uptake reached 133% of theory for $NO_2 \longrightarrow NH_2$. The cooled solution deposited 1-*p*-aminophenoxy-7-phthalimidoheptane (55%), m. p. 107—109° [after recrystallisation from chloroform–light petroleum (b. p. 60—80°)]. Concentration of the mother-liquors afforded the *hexahydro-compound* (27%) which, after recrystallisation from chloroform–light petroleum, had, m. p. 73—75° (Found: C, 70·2; H, 7·9; N, 7·8. $C_{21}H_{30}O_3N_2$ requires C, 70·3; H, 8·4; N, 7·8%).

1-p-*Aminophenoxy*-5-*maleimidopentane*.—1-Maleimido-5-*p*-nitrophenoxypentane (5·9 g.) was added to a solution of stannous chloride dihydrate (18 g.) in warm concentrated hydrochloric acid (27 ml.). The solution was kept for 5 min. at 100°, then slowly poured into a stirred mixture of 50% aqueous sodium hydroxide (50 ml.) and chloroform (100 ml.) maintained at 0°. The chloroform solution was immediately separated, washed, dried, concentrated, and diluted with light petroleum. Recrystallisation of the crystalline product from ethyl acetate–light petroleum gave the *amine* (71%), m. p. 122—124° (Found: C, 64·7; H, 7·2; N, 10·0. $C_{15}H_{18}O_3N_2$ requires C, 65·7; H, 6·6; N, 10·2%). The *methanesulphonate* had m. p. 194—195° (Found: C, 51·4; H, 5·9; N, 7·75; S, 9·1. $C_{15}H_{18}O_3N_2,CH_4O_3S$ requires C, 51·9; H, 6·0; N, 7·6; S, 8·65%) (from ethanol). Both the base and the methanesulphonate gave consistently low carbon analyses.

3-(5-p-*Aminophenoxypentyl*)*rhodanine* (40%), m. p. 104—106° (from ethanol) (Found: C, 54·1; H, 5·9; N, 8·9. $C_{14}H_{18}O_2N_2S_2$ requires C, 54·1; H, 5·8; N, 9·0%), and 3-(5-p-*aminophenoxypentyl*)-5-*benzylidenerhodanine* (73%) (acetic acid used as solvent), m. p. 133—135°

[17] Dirscherl and Weingarten, *Annalen*, 1951, **574**, 137.
[18] Dannerth, *J. Amer. Chem. Soc.*, 1907, **29**, 1319.

(from 2-ethoxyethanol) (Found: C, 63·1; H, 5·4; N, 6·7. $C_{21}H_{22}O_2N_2S_2$ requires C, 63·3; H, 5·5; N, 7·0%), were similarly prepared. 3-(5-p-*Aminophenoxypentyl*)*thiazolidine*-2,4-*dione*, m. p. 107—109° (from ethanol) (Found: C, 57·3; H, 6·1; N, 9·2. $C_{14}H_{18}O_3N_2S$ requires C, 57·2; H, 6·1; N, 9·5%), was prepared (54%) by reducing the corresponding nitro-compound with stannous chloride or, preferably, with reduced iron powder and aqueous acetic acid.

1-p-*Aminophenoxy*-5-*cyanoacetamidopentane*.—A mixture of 1-amino-5-*p*-aminophenoxypentane (14·55 g.), ethyl cyanoacetate (8·36 g.), and methanol (20 ml.) was kept for 5 days in a stoppered flask. The solid was recrystallised from ethanol, giving the *cyanoacetamide* (81%), m. p. 92—93° (Found: C, 64·4; H, 7·2; N, 16·0. $C_{14}H_{19}O_2N_3$ requires C, 64·35; H, 7·2; N, 16·1%). The *acetyl derivative*, m. p. 173—175° (from ethanol) (Found: N, 13·8. $C_{16}H_{21}O_3N_3$ requires N, 13·85%), was also obtained directly from 1-*p*-acetamidophenoxy-5-aminopentane and ethyl cyanoacetate.

Similarly prepared were 1-p-*aminophenoxy*-5-*dichloroacetamidopentane* (experiment by Mr. D. E. Wright) (13%), m. p. 81—82° (from benzene–light petroleum) (Found: N, 9·0; Cl, 23·0. $C_{13}H_{18}O_2N_2Cl_2$ requires N, 9·2; Cl, 23·2%), and 1-p-*aminophenoxy*-5-*trichloroacetamidopentane* (66%), m. p. 97—99° (from ether) (Found: N, 7·9; Cl, 31·65. $C_{13}H_{17}O_2N_2Cl_3$ requires N, 8·2; Cl, 31·4%).

1-p-*Aminophenoxy*-5-*phthalimidinopentane*.—Concentrated hydrochloric acid (100 ml.) was added during 1 hr. to a stirred, refluxing mixture of 1-*p*-aminophenoxy-5-phthalimidopentane (32·4 g.), tin (25 g.) and ethanol (200 ml.). After a further 17 hr. the solution was filtered and the cooled filtrate was slowly added to 50% aqueous sodium hydroxide (200 ml.). The precipitate was filtered off, washed with water, and extracted with boiling ethanol (400 ml.). The cooled extract afforded the *phthalimidine* (63%), m. p. 143—144° (Found: C, 73·7; H, 7·1; N, 8·9. $C_{19}H_{22}O_3N_2$ requires C, 73·5; H, 7·15; N, 9·0%).

Except where stated, the amines in Table 2 were prepared by catalytic reduction of the corresponding nitro-compounds, usually over Raney nickel in ethanol, 2-ethoxyethanol, or dimethylformamide.

N-*Substituted amines*.

1-p-*Dimethylaminophenoxy*-3-*phthalimidopropane*.—1-*p*-Aminophenoxy-3-phthalimidopropane, m. p. 92—93° (prepared by reduction of the nitro-compound; lit.,[19] m. p. 92—94°), was converted by methyl iodide and sodium carbonate in ethanol into the quaternary iodide (100%), m. p. 203—206° (from water), which was pyrolysed under reduced pressure, giving 1-*p*-dimethylaminophenoxy-3-phthalimidopropane (100%), m. p. 121—122° (from ethanol) (Found: C, 70·7; H, 6·3; N, 8·4. Calc. for $C_{19}H_{20}O_3N_2$: C, 70·4; H, 6·2; N, 8·6%) (lit.,[11] m. p. 159·6—160·9°).

1-*Benzenesulphonamido*-5-p-*dimethylaminophenoxypentane*, m. p. 71—72·5° (from ether) (Found: N, 7·5; S, 8·9. $C_{19}H_{26}O_3N_2S$ requires N, 7·7; S, 8·8%), was similarly obtained (96%) from its *methiodide* (96%), m. p. 183—185° (from water) (Found: N, 5·5; I, 25·4. $C_{20}H_{29}O_3N_2SI$ requires N, 5·55; I, 25·15%).

1-(p-N-*Methylacetamidophenoxy*)-5-*phthalimidopentane*, prepared (53%) from *p*-*N*-methylacetamidophenol, 5-phthalimidopentyl bromide, and sodium ethoxide in ethanol, had m. p. 83—85° (from chloroform–ether) (Found: N, 7·6. $C_{22}H_{24}O_4N_2$ requires N, 7·4%). 1-(p-N-*Methylbenzamidophenoxy*)-5-*phthalimidopentane*, m. p. 121—124° (from methanol) (Found: N, 6·2. $C_{27}H_{26}O_4N_2$ requires N, 6·3%), was similarly obtained.

1-*Amino*-5-p-*methylaminophenoxypentane*, prepared by refluxing the foregoing acetyl derivative with concentrated hydrochloric acid, had m. p. 76—79° [from light petroleum (b. p. 60—80°)], b. p. 200—205°/15 mm. (Found: C, 69·2; H, 10·1; N, 13·3. $C_{12}H_{20}ON_2$ requires C, 69·2; H, 9·7; N, 13·4%). It decomposed on storage.

1-*Benzamido*-5-(p-N-*methylacetamidophenoxy*)*pentane*.—The corresponding 5-phthalimido-compound was treated with aqueous-alcoholic hydrazine, as previously described, and the amine formed was benzoylated, yielding the *benzamide* (61% overall), m. p. 110—112° (from acetone–light petroleum) (Found: N, 7·95. $C_{21}H_{26}O_3N_2$ requires N, 7·9%). 1-*Benzamido*-5-(p-N-*methylformamidophenoxy*)*pentane*, m. p. 115—116° (from acetone–ether) (Found: C, 71·05; H, 7·0; N, 8·3. $C_{20}H_{24}O_3N_2$ requires C, 70·4; H, 7·0; N, 8·2%), was similarly prepared (12% overall). Partial hydrolysis of either the *N*-formyl or the *N*-acetyl derivative, with aqueous hydrochloric acid (1 equiv.) in acetic acid, then afforded 1-*benzamido*-5-p-*methylaminophenoxypentane* (60%), m. p. 91—92° (from acetone–light petroleum) (Found: C, 73·5; H, 7·7; N, 8·9.

[19] Matejka and Robinson, *J.*, 1934, 1324.

$C_{19}H_{24}O_2N_2$ requires C, 73·45; H, 7·7; N, 9·0%). The N-*benzoyl derivative* had m. p. 111—113° (from benzene–ether) (Found: C, 75·0; H, 6·3; N, 6·6. $C_{26}H_{28}O_3N_2$ requires C, 75·0; H, 6·8; N, 6·7%).

1-*Benzenesulphonamido*-5-(p-N-*methylacetamidophenoxy*)*pentane*, m. p. 109—111° (from toluene–light petroleum) (Found: N, 7·05; S, 8·4. $C_{20}H_{26}O_4N_2S$ requires N, 7·2; S, 8·2%), was similarly prepared and was hydrolysed to 1-*benzenesulphonamido*-5-p-*methylaminophenoxypentane* (62% overall), m. p. 83—85° (from ethanol) (Found: N, 7·8; S, 9·6. $C_{18}H_{24}O_3N_2S$ requires N, 8·0; S, 9·2%). The latter base, on treatment with ethylene chlorohydrin and calcium carbonate in boiling water, yielded 1-*benzenesulphonamido*-5-[p-(2-*hydroxy*-N-*methylethylamino*)*phenoxy*]*pentane* (76%), m. p. 76—78° (from benzene–light petroleum) (Found: N, 6·95; S, 8·3. $C_{20}H_{28}O_4N_2S$ requires N, 7·1; S, 8·2%).

1,2-*Di*-(p-5-*benzamidopentyloxyanilino*)*ethane*.—A mixture of 1-*p*-aminophenoxy-5-benzamidopentane (14·9 g.), ethylene dibromide (4·7 g.), and ethanol (25 ml.) was refluxed for 20 hr., cooled, and filtered. The solid was extracted with water and boiling ethanol. The insoluble residue was the piperazine derivative (3·3 g., see below). The ethanolic extract yielded the *dianilinoethane* (24%), m. p. 155—157° (from ethanol) (Found: C, 73·1; H, 7·5; N, 8·9. $C_{38}H_{46}O_4N_4$ requires C, 73·3; H, 7·45; N, 9·0%).

1,4-*Di*-(p-5-*benzamidopentyloxyphenyl*)*piperazine*.—The foregoing dianilinoethane (8·1 g.), ethylene dibromide (4·7 g.), and sodium hydrogen carbonate (4·2 g.) were refluxed in 2-ethoxyethanol (30 ml.) for 20 hr. The *piperazine* formed (96%) had m. p. 231—233° (from 2-ethoxyethanol) (Found: C, 74·15; H, 7·3; N, 8·6. $C_{40}H_{48}O_4N_4$ requires C, 74·1; H, 7·45; N, 8·6%).

1-p-*Di*-(2-*chloroethyl*)*aminophenoxy*-5-*phthalimidopentane*.—Phosphorus oxychloride (2·74 ml.), was added to 1-*p*-di-(2-hydroxyethyl)aminophenoxy-5-phthalimidopentane (B.P. 769,706) (4·12 g.) in dry benzene (15 ml.) and the mixture was refluxed for 2 hr., poured on ice and extracted with benzene. The washed and dried extract was evaporated and the residue was triturated with ether. Crystallisation of the product from ethanol gave the *chloroethyl derivative* (81%), m. p. 107—108° (Found: N, 6·2; Cl, 15·5. $C_{23}H_{26}O_3N_2Cl_2$ requires N, 6·2; Cl, 15·8%).

1-(3-*Chloro*-p-*tolyl*)-4-(p-5-*phthalimidopentyloxyphenyl*)*piperazine*.—A mixture of the foregoing chloroethyl compound (17·96 g.), 3-chloro-*p*-toluidine (5·66 g.), sodium carbonate (4·24 g.), and 2-ethoxyethanol (75 ml.) was refluxed for 20 hr., cooled, and filtered. The solid product was washed with water and crystallised from chloroform–ethanol, yielding the *piperazine* (63%), m. p. 149—150° (Found: N, 8·2; Cl, 6·7. $C_{30}H_{32}O_3N_3Cl$ requires N, 8·1; Cl, 6·8%).

1-p-(2-*Amino*-6-*methylpyrimid*-4-*ylamino*)*phenoxy*-5-*phthalimidopentane*.—A mixture of 2-amino-4-chloro-6-methylpyrimidine (14·35 g.), 1-*p*-aminophenoxy-5-phthalimidopentane (32·4 g.), N-hydrochloric acid (100 ml.), and water (500 ml.) was refluxed for 1 hr., cooled, and made just alkaline to phenolphthalein. Recrystallisation of the solid product from 2-ethoxyethanol gave the *pyrimidine derivative* (67%), m. p. 211—213° (Found: C, 66·9; H, 5·8; N, 15·9. $C_{24}H_{25}O_3N_5$ requires C, 66·8; H, 5·8; N, 16·2%). Treatment with methyl sulphate in nitrobenzene for 1 hr. at 100° afforded the 1-*metho*(*methyl sulphate*) (75%), m. p. 186—188° (from ethanol) (Found: N, 12·8; S, 6·2. $C_{26}H_{31}O_7N_5S$ requires N, 12·5; S, 5·8%).

4-*Amidino*-4′-(5-*phthalimidopentyloxy*)*diazoaminobenzene*.—A solution of sodium nitrite (1·43 g.) in water (24 ml.) was added slowly at 0—5° to a mixture of *p*-aminobenzamidine dihydrochloride (4·16 g.) and concentrated hydrochloric acid (2·9 ml.) in water (17 ml.). The resulting solution was stirred whilst a solution of 1-*p*-aminophenoxy-5-phthalimidopentane (6·28 g.) in acetic acid (20 ml.) (at 20°) was quickly added, followed immediately by saturated sodium acetate. The red precipitate was filtered off, washed with water, and recrystallised from ethanol, giving the *amidine acetate* (68%), m. p. 210—212° (Found: C, 63·3; H, 6·4; N, 15·8. $C_{26}H_{26}O_3N_6,C_2H_4O_2$ requires C, 63·4; H, 5·7; N, 15·8%).

5-*Benzamido*-1-p-*carbamoylmethylaminophenoxypentane*.—A mixture of 1-*p*-aminophenoxy-5-benzamidopentane (19·7 g.), chloroacetamide (6·18 g.), sodium carbonate (3·5 g.), and ethanol (200 ml.) was refluxed for 20 hr., cooled, diluted with water, and filtered. Crystallisation of the product from ethanol gave the *amide* (61%), m. p. 161—163° (Found: C, 68·0; H, 6·6; N, 11·6. $C_{20}H_{25}O_3N_3$ requires C, 67·6; H, 7·1; N, 11·8%).

1-p-D-*Glucosylaminophenoxy*-5-*phthalimidopentane*.—A solution of 1-*p*-aminophenoxy-5-phthalimidopentane (3·24 g.), D-glucose (1·8 g.), and 5% ethanolic calcium chloride (0·5 ml.) in ethanol (20 ml.) was refluxed for 1·5 hr., cooled, and filtered. The *glucosylamine* (86%) had m. p. 110—115° (Found: C, 60·1; H, 6·55; N, 5·6; H_2O, 3·7. $C_{25}H_{30}O_8N_2,H_2O$ requires C, 59·5; H, 6·4; N, 5·55; H_2O, 3·6%).

1-*Benzamido*-5-p-D-*glucosylaminopentane* (83%), m. p. 119—120° (from aqueous methanol) (Found: C, 61·25; H, 7·3; N, 6·0; H_2O, 2·0. $C_{24}H_{32}O_7N_2,0{\cdot}5H_2O$ requires C, 61·4; H, 7·1; N, 6·0; H_2O, 1·9%), was similarly prepared.

Miscellaneous compounds.

4-(3-*Chloro*-p-*tolyl*)-1-(5-p-*nitrophenoxypentyl*)*piperazine*.—A mixture of 5-*p*-nitrophenoxypentyl bromide (14·6 g.), 1-(3-chloro-*p*-tolyl)piperazine [20] (10·65 g.), and ethanol (75 ml.) was refluxed for 40 hr., cooled, and filtered from the *hydrobromide* (76%), m. p. 170—172° (from ethanol) (Found: N, 8·3. $C_{22}H_{28}O_3N_3Cl,HBr$ requires N, 8·4%), of the product. The free *base* had m. p. 101—103° (from ethanol) (Found: N, 10·1; Cl, 8·6. $C_{22}H_{28}O_3N_3Cl$. requires N, 10·05; Cl, 8·5%). Reduction with sodium sulphide gave **1-(5-p-*aminophenoxypentyl*)-4-(3-*chloro*-p-*tolyl*)*piperazine*** (86%), m. p. 95—96° (from ethanol) (Found: N, 10·9; Cl, 9·0. $C_{22}H_{30}ON_3Cl$ requires N, 10·8; Cl, 9·15%).

1,4-*Di*-(5-p-*nitrophenoxypentyl*)*piperazine*.—A mixture of 5-*p*-nitrophenoxypentyl bromide (5·76 g.) and piperazine hexahydrate (1·94 g.) was heated for 40 hr. at 100°. Refluxing the residue with ethanol afforded the sparingly soluble *dihydrobromide* (92%), m. p. 253—255° (Found: N, 8·3; Br, 24·5. $C_{26}H_{36}O_6N_4,2HBr$ requires N, 8·45; Br, 24·2%). The light-sensitive *base* had m. p. 122—123° (from ethanol) (Found: C, 62·2; H, 7·6; N, 11·2. $C_{26}H_{36}O_6N_4$ requires C, 62·4; H, 7·25; N, 11·2%). Catalytic reduction yielded **1,4-*di*-(5-p-*aminophenoxypentyl*)*piperazine*** (92%), m. p. 124—126° [from ethanol–light petroleum (b. p. 100—120°)] (Found: C, 70·3; H, 9·5; N, 12·5. $C_{26}H_{40}O_2N_4$ requires C, 70·85; H, 9·2; N, 12·7%).

A further group of compounds, prepared by standard methods, and not described previously, is recorded in Table 3.

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[20] Farbwerke Hoechst A.G., Belgian Patent 539,950.

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784. *Nitration of Alcohols at Oxygen Centres. Part I. Criteria for the Nitronium-ion Mechanism in Aqueous Solutions of Strong Acids.*

By T. G. BONNER and D. E. FRIZEL.

The correlation of nitration rates in aqueous sulphuric acid with the acidity function, C_0, as a criterion of nitronium-ion mechanism is discussed. A new criterion for this mechanism in aqueous perchloric acid is put forward based on the ionisation of nitrous acid to the nitrosonium ion in this medium and its extension to sulphuric acid is considered. Comparison is made with the ionisation of certain triphenylmethanol-type indicators and in one case ionisation measurements in perchloric acid are reported for the first time.

THE elegant test for the operation of the nitronium mechanism in *C*-,[1] *N*-, and *O*-nitration [2,3] based on the demonstration of zeroth-order kinetics for sufficiently reactive substrates is decisive in the case of nitration by excess of nitric acid in a relatively weak acidic environment. Under such conditions the rate-controlling step becomes the dissociation of the nitric acidium ion $H_2NO_3^+$ to nitronium ion, NO_2^+ (nitryl cation), which is consumed rapidly and completely by the substrate. In a strongly acidic solvent this test is inapplicable as the nitronium ion is formed in a rapidly established equilibrium, and although its

[1] Hughes, Ingold, and Reed, *J.*, 1950, 2400.
[2] Blackall and Hughes, *Nature*, 1952, **170**, 972.
[3] Hughes, Ingold, and Pearson, *J.*, 1958, 4357; Blackall, Hughes, Ingold, and Pearson, *J.*, 1958, 4366.

presence can be inferred and its potency assumed there is the necessity of proving that it is the active nitrating agent in this particular situation, particularly since it may be present in such minute concentrations that direct detection by physical methods is impossible.

A valuable criterion for the nitronium-ion mechanism in aromatic *C*-nitration in 80—90% sulphuric acid is the parallelism existing between the experimental rate constant of nitration, k, and the ionisation of a triphenylmethanol, ZOH, to its carbonium ion Z^+, which is based on the similarity in the mode of ionisation of nitric acid and triphenylmethanol: [4]

$$HNO_3 + 2H_2SO_4 \rightleftharpoons NO_2^+ + H_3O^+ + 2HSO_4^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$ZOH + 2H_2SO_4 \rightleftharpoons Z^+ + H_3O^+ + 2HSO_4^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

This method was extended to a wider range of sulphuric acid–water mixtures by means of eqn. (3) which applies to any single sulphuric acid solvent in which each base is present

$$pK_{ZOH} - pK_{HNO_3} = \log([Z^+]/[ZOH]) - \log([NO_2^+]/[HNO_3]) + \log(f_{Z^+} f_{HNO_3}/f_{NO_2^+} f_{ZOH}) \quad . \quad (3)$$

only in the cationic and neutral forms indicated.[5] K_{HNO_3} and K_{ZOH} are the thermodynamic equilibrium constants for the ionisations (1) and (2) and the f terms represent activity coefficients. The derivation of a useful relationship between k and the ionisation ratio $[Z^+]/[ZOH]$ depends on the constancy of the activity-coefficient ratio in (3) over a sufficiently wide range of sulphuric acid–water mixtures. Although direct demonstration of this constancy is not impossible since there is no analytical method of determining the ratio $[NO_2^+]/[HNO_3]$ independently, it was shown that the plots of $\log([Z^+]/[ZOH])$ for four different triphenylmethanol indicators against the percentage of sulphuric acid gave approximately straight lines which were reasonably parallel [6] and covered the range 65—90% sulphuric acid. This implies that the variation of $\log(f_{Z^+}/f_{ZOH})$ with composition of the medium is the same for each indicator. If it is assumed that the variation of $\log(f_{NO_2^+}/f_{HNO_3})$ with medium composition would be very similar, it follows that the difference in the log (ionisation ratio) terms in (3) is constant and independent of the medium and that in the region of acidity where the extent of ionisation of nitric acid to nitronium ion is small (*i.e.*, below about 86% sulphuric acid [7]), k is related to $[Z^+]/[ZOH]$ by eqn. (4).

$$\log k - \log([Z^+]/[ZOH]) = \text{Constant} \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

The application of eqn. (4) to *C*-nitration of the trimethyl-*p*-tolylammonium ion,[5] and to *N*-nitration of guanidine [8] and of methylnitroguanidine,[9] covering the range 71—82% sulphuric acid resulted in gradients of −1·20, −1·06, and −0·93 respectively for the plots of log k against log $([Z^+]/[ZOH])$. Although there is some spread of values around the theoretical value of unity, they are taken to prove that these reactions proceed through the nitronium-ion mechanism. The nitric acidium ion $H_2NO_3^+$ was excluded in all cases since there was no evidence for the correlation of k with the Hammett acidity function H_0 according to eqn. (5) which would be applicable in this event.

$$\log k + H_0 = \text{Constant} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

More useful general forms of eqn. (4) are based on the definition of acidity functions, *viz.*,

[4] Westheimer and Kharasch, *J. Amer. Chem. Soc.*, 1946, **68**, 1871.
[5] Lowen, Murray, and Williams, *J.*, 1950, 3318.
[6] Murray and Williams, *J.*, 1950, 3322.
[7] Bonner and Williams, *Chem. and Ind.*, 1951, 820.
[8] Simkins and Williams, *J.*, 1953, 1386.
[9] Hardy-Klein, *J.*, 1957, 70.

H_R,[5] J_0,[10] and C_0 [11] related to the ionisation of triphenylmethanol indicators. They are of the type shown in eqn. (6), which appears to have received the widest application.

$$\log k + C_0 = \text{Constant} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

where $$C_0 = pK_{ZOH} - \log([Z^+]/[ZOH]) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

C_0 has been evaluated for the almost complete range of sulphuric acid–water mixtures by using a large number of indicators ionising according to eqn. (2), not all of which are triphenylmethanol derivatives. In applying this acidity function to the examination of nitration data, Deno and Stein tested eqn. (6) in the differentiated form (8):

$$d\ C_0/d\ \%H_2SO_4 = -d \log k/d\ \%H_2SO_4 \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

or alternatively $$d \log Q/d\ \%H_2SO_4 = d \log k/d\ \%H_2SO_4 \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

where $Q = [Z^+]/[ZOH]$ with the implication that the gradients in (8) and (9) are determined for overlapping ranges of indicator ionisation and nitration measurement. In testing eqn. (8), Deno and Stein [12] found some serious weaknesses in this general method of analysing nitration results. $d\ C_0/d\ \%H_2SO_4$ changes from 0·12 in mixtures containing up to 25% sulphuric acid to a value of 0·26 over the range 60—90% sulphuric acid. Above 90% sulphuric acid, the value increased still further to 0·34. This variation in itself would not be objectionable provided that (*a*) the value of $d\ C_0/d\ \%H_2SO_4$ over the fixed range in which nitration rates are being measured is independent of the indicator selected for evaluation of C_0 in this range, and (*b*) over fixed ranges of medium composition, *e.g.*, 0—10%, 10—20%, 20—30%, etc., sulphuric acid, the gradient maintained a characteristic value not varying by more than, say, ±5%.

The evidence concerning condition (*a*) is conflicting. Table 1 gives the value of

TABLE 1.

Indicator	$\%H_2SO_4$	$d \log Q/d\ \%H_2SO_4$
(I) 2-Phenylborneol [a]	58—68	0·25
(II) 3,3′,3″-Trichlorotriphenylmethanol [a]	64—72	0·25—0·26
(III) Chloro-4,4′-dinitrotriphenylmethane [a]	70—78	0·26—0·27
(IV) 4,4′,4″-Trinitrotriphenylmethanol [a]	84—92	0·26
(V) Methyl 4-trimethylammoniumphenylmethyl ether perchlorate [b]	58—66	0·26
(VI) 4,4′-Bis(trimethylammonium)triphenylmethyl methyl ether diperchlorate [c]	66—74	0·29
(VII) 4-Chloro-4′,4″-bis(trimethylammonium)triphenylmethyl methyl ether diperchlorate [b]	67—76	0·33
(VIII) Methyl 4,4′,4″-tris(trimethylammonium)triphenylmethyl ether triperchlorate [c]	79—85	0·34
(XI) 4,4′,4″-Tris(trimethylammonium)triphenylmethyl triperchlorate [c]	79—85	0·37
(IV) 4,4′,4″-Trinitrotriphenylmethanol [c]	83—91	0·30

[a] Ref. 11. [b] Ref. 13. [c] Ref. 6.

$d \log Q/d\ \%H_2SO_4$ for four indicators (I—IV) reported by Deno *et al.*[11] and six (IV–IX) by Williams *et al.*[6,13] which collectively cover the range 60—90% sulphuric acid. The differences in the values of the gradients between the two groups are apparent; in addition, the results for (IV) which is common to both groups differ appreciably. In a detailed examination of the applicability of eqn. (8) to nitration data, Deno and Stein [12] found that the equality of the gradients for $\log k$ and C_0 was maintained up to 62% sulphuric acid but above this acidity considerable divergence ensued, *e.g.*, for the nitration of nitrobenzene in 80—87·5% sulphuric acid the value of $d \log k/d\ \%H_2SO_4$ is 0·39 while $d\ C_0/d\ \%H_2SO_4$ is 0·26. The previously employed test of the nitronium-ion mechanism with eqn. (4) or (6) would give a satisfactory result of 1·18 for the slope of $\log k$ against $\log Q$ for indicator

[10] Gold and Hawes, *J.*, 1951, 2102; Gold, *J.*, 1955, 1263.
[11] Deno, Jaruzelski, and Schriesheim, *J. Amer. Chem. Soc.*, 1955, **77**, 3044.
[12] Deno and Stein, *ibid.*, 1956, **78**, 578.

(VIII) but the less acceptable result of 1·50 for the similar plot of log k against C_0. Differences in ionisation characteristics of the type evident in Table 1 are usually attributed to a difference in the activity coefficient functions d log (f_{Z^+}/f_{ZOH})/d $\%H_2SO_4$ arising from variation in charge type or molecular size. The difficulty of prediction in this matter is evident from the fact that while there are marked differences between the singly, doubly, and triply charged types of the lower group there are none between the uncharged types of the upper group and the singly charged indicator (V). It is possible that this factor may depend on the range of media in which comparisons are made and it has been pointed out that activity coefficients of a variety of oxygen-containing compounds change rapidly over the range 65—80% sulphuric acid.[12] This may be a particularly vulnerable region but the deviations are also apparent in higher acidities and it has been recently shown for certain compounds that d (log f)/d $\%H_2SO_4$ changes very rapidly above 80% sulphuric acid.[14]

A closer examination of the published data on the ionisation of the indicators (IV), (VI), (VII), and (IX) in the lower group of Table 1 suggests that the other condition (*b*) is also not very satisfactorily fulfilled. The plots of log Q against the percentage of sulphuric acid all show a distinct curvature corresponding to a marked change in gradient over even smaller ranges of media than the arbitrarily chosen 10% range. The variation in gradient with range of media is shown in Table 2. In the case of (VIII) the marked curvature

TABLE 2.

Indicator	(VI)		(VIII)		(IX)		(IV)	
$\%H_2SO_4$	65—71	70—74	80—82	82—85	80—82	82—85	83—87	87—90
d log Q/d $\%H_2SO_4$	0·26	0·34	0·33	0·36	0·36	0·39	0·33	0·26

evident at very low ionisation has been dismissed as insignificant [5] but although this view may be erroneous this part of the curve has not been used in calculating the data for (VIII) in Table 2. The greater precision which has been achieved [15] in the determination of [Z⁺]/[ZOH] values confirms the conclusions implicit in Table 2. Although the limited results reported [11] for indicators used in the evaluation of the C_0 scale do not show the same wide variations it was noted that certain indicators showed a lack of constancy in this property and these were rejected as unsuitable.

The failure of d log Q/d $\%H_2SO_4$ to possess the same value for different indicators, or even to maintain for many individual indicators the constancy required to provide a useful test for the nitronium-ion mechanism, indicates the uncertainty involved in assuming that d log (f_{R^+}/f_{ROH})/d $\%H_2SO_4$ is the same for all compounds ionising according to eqns. (2) or (3). The degree of success of equations (4), (6), (8), or (9) in diagnosing a nitronium-ion mechanism is clearly controlled by the choice of compound for the measurement of [Z⁺]/[ZOH] ratios over the range where nitration rates have been measured.

The need to compare nitration rates with the ionisation of a compound as closely similar in size and structure as possible to nitric acid is evident. This became possible with reports of the determination of the extent of ionisation in aqueous perchloric acid of nitrous acid to the nitrosonium (nitrosyl) ion NO^+ according to eqn. (10) [16] and similarly in

$$HNO_2 + 2HClO_4 \rightleftharpoons NO^+ + H_3O^+ + 2ClO_4^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

aqueous sulphuric acid.[17] As a result of these reports, data were available on the ionisation ratio $[NO^+]/[HNO_2]$ over the range 45—56% perchloric acid and 50—75% sulphuric acid. Several alcohols were investigated to select a suitable one for measurement of *O*-nitration rates in a near or overlapping range of media, and isopentyl alcohol was found to be the most satisfactory. It is rapidly and almost quantitatively converted into its nitrate ester

[13] Williams and Bevan, *Chem. and Ind.*, 1955, 171.
[14] Deno and Perizollo, *J. Amer. Chem. Soc.*, 1957, **79**, 1345.
[15] Bevan, unpublished work.
[16] Singer and Vamplew, *J.*, 1956, 3971.
[17] Bayliss and Watts, *Austral. J. Chem.*, 1956, **9**, 319.

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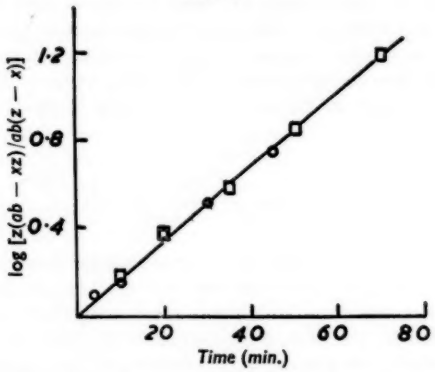
with a mixture of nitric and sulphuric acid at 0° with no apparent oxidation.[18] At 0° and 25° measurable rates of nitration were obtained within the range of 57—75% sulphuric acid with attainment of an unchanging equilibrium in a reasonably short time. The comparable range for perchloric acid at 25° was 55—62·5% acid. In both media, the extremely small amount of oxidation of the alcohol which was detected was eliminated by addition of 0·001M-sulphamic acid. With fixed initial concentrations of isopentyl alcohol (0·07M) and nitric acid (0·15M) the experimental rate equation corresponded to a second-order forward reaction (the *O*-nitration) opposed by a first-order reverse reaction (hydrolysis of isopentyl nitrate). The nitration rate constant, k, was calculated from eqn. (11) where

$$kt\,(ab - z^2) = 2{\cdot}3\,z \log [z(ab - zx)/ab\,(z - x)] \quad . \quad . \quad . \quad (11)$$

a and b are the initial concentrations of nitric acid and isopentyl alcohol and x and z are the concentrations of isopentyl nitrate at time t (minutes) and at equilibrium respectively.

FIG. 1.



In all rate measurements the plot of log $[z(ab - zx)/ab(z - x)]$ against t was a straight line from the slope of which k was calculated (see Fig. 1 for a duplicated typical experi-

TABLE 3. *Rates of* O*-nitration of isopentyl alcohol.*

Initial [isopentyl alcohol] = 0·07M; [HNO_3] = 0·15M

Perchloric acid at 25°.							
%$HClO_4$	62	60·8	59·3	58·0	56·3	55·2	
k	1·56	0·71	0·275	0·100	0·051	0·0222	
	1·58	0·72	0·267	0·102	0·049	0·0225	
Ester (%)	54	46	38	34	28	25	
Sulphuric acid at 25°.							
%H_2SO_4	67·0	66·0	65·3	63·5	62·4	60·0	57·7
k	0·312	0·254	0·218	0·095	0·051	0·0170	0·0074
	0·318	0·249	0·221	0·093	0·049	0·0174	0·0072
Ester (%)	65	68	66	56	48	42	38
Sulphuric acid at 0°							
%H_2SO_4	74·6	72·7	71·4	69·7	68·0	64·6	
k	1·53	0·59	0·343	0·088	0·0351	0·0059	
	1·46	0·60	0·348	0·086	0·0340	0·0060	
Ester (%)	66	63	62	59	55	49	

k is the rate constant obtained graphically from eqn. (11). Ester (%) refers to the percentage conversion of isopentyl alcohol into isopentyl nitrate at equilibrium.

ment). The rate constants obtained for *O*-nitration in aqueous perchloric acid and sulphuric acid are given in Table 3 together with the percentage conversion of the alcohol into nitrate

[18] Chapman and Smith, *J.*, 1867, 581; Boschan, Merrow, and van Dolah, *Chem. Rev.*, 1955, **55**, 485.

at equilibrium. The test for the nitronium-ion mechanism in perchloric acid is that equation (12) should be satisfied, it being assumed that d log $(f_{NO_2^+}/f_{HNO_2})$/d %$HClO_4$ and

$$\text{d log } k/\text{d \%}HClO_4 = \text{d log } (NO^+/HNO_2)/\text{d \%}HClO_4 \quad . \quad . \quad . \quad (12)$$

d log (f_{NO^+}/f_{HNO_2})/d %$HClO_4$ are closely similar. The plots of log k and of log $([NO^+]/[HNO_2])$ against percentage of perchloric acid are shown in Fig. 2. The best line through each set of points being taken, both gradients are 0·27. It is possible to discern a slight curvature in the plot of log k, and if this is assumed to be real an increase in gradient from 0·27 to 0·30 with increasing acidity is evident. Discounting the highest point on the log $[NO^+]/[HNO_2]$ line, since it corresponds to more than 95% ionisation and is therefore liable to considerable inaccuracy, we cannot decide, with the limited data, whether any similar curvature occurs in this case. It is clear, however, that in the absence of more accurate

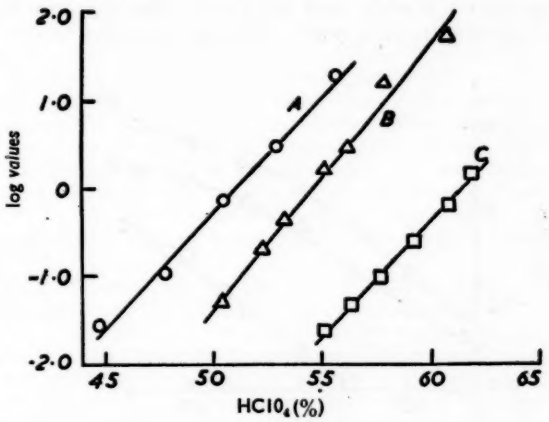


FIG. 2.
A, Plot of log $([NO^+]/[HNO_2])$; slope 0·27.
B, Plot of log $([Z^+]/[ZOH])$; slope 0·31.
C, Plot of log k; slope 0·27.

ionisation measurements the correspondence required by eqn. (12) and by the similar equations (4), (6), (8), and (9) may not be closer than 10% even in the most favourable circumstances. For comparison, some ionisation ratios for indicator (V) (Table 1) were measured in 50—56% perchloric acid and log $([Z^+]/[ZOH])$ is included in Fig. 2. Again, more data are desirable bnt thé best line has a gradient of 0·31 which is close enough to that of the log k value to provide an acceptable proof of the nitronium-ion mechanism. Divergences of this order have been recognised for some time in applications of eqn. (5).[19]

The application of a similar equation to (12) to the results obtained in sulphuric acid is more complicated. Bayliss and Watts [17] do not mention the difficulties noted in this medium by Singer and Vamplew [16] of (i) a large shift in the position of the maximum in the absorption spectrum of the nitrosonium ion with change in acidity, and (ii) appreciable loss of nitrous acid in aqueous acid solutions; these difficulties led the latter authors to abandon sulphuric acid in favour of perchloric acid for their studies. Further, although the latter authors found no evidence in perchloric acid for a third entity such as $H_2NO_2^+$, since the sum of the nitrosonium ion and molecular nitrous acid concentrations corresponded to the initial amount of nitrous acid determined by chemical analysis, Bayliss and Watts found a discrepancy between the two amounts which rose to a maximum between 50% and 65% sulphuric acid which they accounted for by postulating the existence of the $H_2NO_2^+$ ion. In view of this uncertainty about the composition of nitrous acid solutions in sulphuric acid, two different procedures have been employed to obtain

[19] Long and McIntyre, *J. Amer. Chem. Soc.*, 1954, **76**, 3240; Long and Paul, *Chem. Rev.*, 1957, **57**, 935.

d log (NO^+/HNO_2)/d $\%H_2SO_4$; first, values of log $[NO^+]/[HNO_2]$ were calculated in which $[HNO_2]$ was the figure quoted as the concentration of molecular nitrous acid found directly by absorption spectra measurement. Secondly, log $([NO^+]/[HNO_2)_T)$ was evaluated, where $[HNO_2]_T$ is the sum of the values given for $[HNO_2]$ and $[H_2NO_2^+]$, *i.e.*, the figure obtained by subtracting the spectroscopically determined NO^+ from the initial total nitrous acid concentration; this is in effect what the molecular nitrous acid concentration would be if no $H_2NO_2^+$ or any other third form of nitrous acid were present. As shown in Fig. 3, in both cases the plot of log (ionisation ratio) against the percentage of sulphuric acid follows the same course; a straight line is obtained over the range 50—62% sulphuric acid over which the ionisation to nitrosonium ion increases to 60%, followed by a sharp change of slope at higher acidities where the rapid increase in conversion of nitrous acid into nitrosonium ion increases the error in evaluating the ionisation ratio. The significant result is that over the range 50—62% sulphuric acid the gradients for log $([NO^+]/[HNO_2])$ and log $([NO^+]/[HNO_2]_T)$ are 0·19 and 0·17 respectively while d log k/d $\%H_2SO_4$ is 0·19. Although there may be some uncertainty in the interpretation

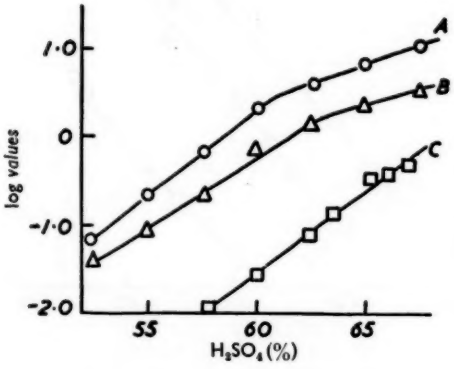


FIG. 3.

A, Plot of log $([NO^+]/[HNO_2])$; slope 0·19 (52—60% H_2SO_4).
B, Plot of log $\{[NO^+]/[H_2NO_2^+] + [HNO_2]\}$; slope 0·17 (52—60% H_2SO_4).
C, Plot of log k; slope 0·19.

of the ionisation data, the closeness of these values is acceptable evidence of the nitronium-ion mechanism for this region of sulphuric acid–water mixtures. A comparison of the nitration rates with the ionisation ratios of triphenylmethanol type indicators shows that much greater divergences exist, since both d C_0/d $\%H_2SO_4$ and d log $Q/\%H_2SO_4$ for indicator (V) have a value of 0·26; otherwise expressed, a plot of log k against C_0 [or log Q for (V)] would have a gradient of 0·64 instead of unity. It is a coincidence that at 0° d log k/d $\%H_2SO_4$ is 0·25, and this large difference from the value at 25° underlies the necessity, often disregarded, of comparing kinetic and ionisation data at the same temperature.

One conclusion which may be drawn from the diagnostic value of equations (4), (6), (8), and (9) in perchloric acid as compared with the large divergences in sulphuric acid is that effects of the medium operate much more strongly in the latter. This difference in behaviour of the solvent has already been observed in the denitration of nitroguanidines in the two acids, and led to the view that in sulphuric acid alone solvent species participated in the transition state of denitration.[20] The shifting of absorption bands characteristic of the nitrosonium ion with change of medium in sulphuric acid and the absence of this effect in perchloric acid [16] is further evidence of the contrast between these solvents. A comparison of the ionisation characteristics of a number of triphenylmethanol-type indicators in perchloric acid would obviously be useful in comparing the extent of the variation of log (f_{Z^+}/f_{ZOH}) with medium composition with that in sulphuric acid.

[20] Bonner and Lockhart, *J.*, 1958, 3852.

Experimental

Materials and Media.—Commercial isopentyl alcohol was repeatedly distilled (b. p. 130°). Isopentyl nitrate was prepared by the gradual addition of isopentyl alcohol to a 1 : 3 (v/v) mixture of concentrated nitric acid and concentrated sulphuric acid at 0°. After the separation of an oily layer in a few minutes, the mixture was poured into a large volume of water. The oil was extracted with ether and the ether solution dried and distilled. The yield of isopentyl nitrate was 95%, and the b. p. 147°.

Sulphuric and perchloric acid media were obtained by dilution of the " AnalaR " concentrated solutions and standardised with N-sodium hydroxide referred through N-hydrochloric acid to potassium iodate and to potassium hydrogen phthalate as standards. The strengths of the acids are given to the nearest 0·1%. Anhydrous nitric acid was prepared as required by distillation under reduced pressure from a 2 : 3 (v/v) mixture of concentrated nitric and concentrated sulphuric acid.

Analysis of Reaction Mixtures.—Measurements with a Hilger Uvispek instrument in aqueous solution showed that absorption by isopentyl alcohol was negligible while with isopentyl nitrate the absorption steadily decreased from $\varepsilon = 33$ at 2400 Å to $\varepsilon = 1{\cdot}54$ at 3800 Å with no maxima. Isopentyl nitrate could be virtually completely extracted from a dilute aqueous acid solution in one operation by hexane and the residual solution analysed for nitrate ion ($\varepsilon = 7{\cdot}1$ at 2940 Å). Solvent interaction with isopentyl alcohol only became noticeable in very strongly acid solutions and was not detectable in the time taken to attain nitration equilibrium in the strongest acids used for rate measurement, *viz.*, 75% sulphuric acid and 62·5% perchloric acid. Very slight oxidation of the alcohol in those acids was detected by small changes in absorption and was completely eliminated without side effects by the addition of 0·001M-sulphamic acid. The rate constants for *O*-nitration in 75% sulphuric acid in the presence and in the absence of sulphamic acid were 1·46 and 1·55 respectively.

To confirm that the reaction being followed was an uncomplicated *O*-nitration one preparative experiment was carried out at 0° in 72·7% sulphuric with initial concentrations of 1M-nitric acid and 0·5M-isopentyl alcohol, *i.e.*, 7 times larger than those used in kinetic measurements. After 15 min. (the time indicated in the kinetic run for the attainment of equilibrium the mixture was added to 200 ml. of water and the oily product extracted with hexane. After drying and removal of the hexane, the residual oil corresponded to a 65% yield of isopentyl nitrate; the yield indicated by analysis of the equilibrium mixture in the kinetic run was 63%. On distillation the whole of the oil distilled at 145°. The failure of hexane to extract isopentyl alcohol from the aqueous acid solution was shown by separately shaking a solution of 1 g. of isopentyl alcohol in 50 ml. of 25% sulphuric acid with 10 ml. of hexane and drying and distilling the hexane extract. The residue weighed less than 50 mg.

Kinetic Measurements.—All rates were determined at 0° and 25° for sulphuric acid and at 25° for perchloric acid solutions with initial concentrations of 0·07M-isopentyl alcohol and 0·15M-nitric acid. Solutions of 0·001M-sulphamic acid and 0·3M-nitric acid were separately prepared in the acid medium at the thermostat temperature (0° or 25°). 20 ml. of the sulphamic acid solution were transferred to the reaction vessel, and the required amount of isopentyl alcohol was added. The reaction was started by delivering 20 ml. of the nitric acid solution from a pipette into the alcohol solution, zero time corresponding to the moment the addition started. 5 ml. samples of the reaction mixture were removed at appropriate intervals and quenched by running them into 10 ml. of distilled water cooled in ice. The solution was shaken with 10 ml. of hexane, and the aqueous layer separated and analysed by measuring the absorption at 2940 Å with the Hilger Uvispek instrument. The amount of nitric acid present was found by comparing this reading with that obtained by treating 5 ml. of the original nitric acid solution in the same way. A check was provided by similar absorption measurement of a solution of potassium nitrate in 70% sulphuric acid diluted in the same manner.

Ionisation of Methyl 4-Methylammoniumtriphenylmethyl Ether Perchlorate in Perchloric Acid.—A pure sample was available.[13] The extent of ionisation to the carbonium ion was about 5% in 50% perchloric acid and was complete in the 64·2% acid with maximum absorption at 4420 Å (ε 34,000). The ionisation ratios $[Z^+]/[ZOH]$ at intermediate acidities were evaluated by the usual procedure [6] and the log Q values are plotted in Fig. 2.

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785. *Nitration of Alcohols at Oxygen Centres. Part II.*[1] *The Equilibria established in Aqueous Sulphuric and Perchloric Acids and the Mechanism of Hydrolysis of the Nitrate Ester.*

By T. G. Bonner and D. E. Frizel.

The extent of conversion of 2,4-dinitrobenzyl alcohol into its nitrate and sulphate esters in *O*-nitration experiments in a wide range of sulphuric acid–water mixtures has been measured. Similar experiments with isopentyl alcohol have indicated a mechanism for the hydrolysis of isopentyl nitrate in both aqueous sulphuric and perchloric acid. A relationship between the equilibrium constant, K_N, for *O*-nitration and functions which are a measure of the acidity of the media is deduced and tested.

The conversion of alcohols into their nitrate esters in high yields can frequently be accomplished by means of nitric acid–sulphuric acid–water mixtures.[2] Numerous studies on hydroxy-compounds have demonstrated both the influence of solvent composition on the yield of nitrate ester and the occurrence of the oxidation and sulphation side reactions.[3] The sulphation in the absence of nitric acid has recently been the subject of a detailed kinetic study in which 2,4-dinitrobenzyl alcohol and ethyl alcohol have been employed.[4] 2,4-Dinitrobenzyl alcohol was suitable for *O*-nitration since unlike ethyl alcohol it was completely resistant to oxidation in the mixed acid. Preliminary experiments on the composition of the equilibrium mixture formed by 0·1M initial concentrations of the alcohol and nitric acid in the range 79—93% sulphuric acid showed that the amount of alcohol consumed was only slightly greater than that converted into the sulphate ester.[4] It was therefore necessary to determine the nitrate ester independently and this was achieved by first oxidising the unchanged alcohol quantitatively with acidic dichromate[3] and then extracting the nitrate ester with an organic solvent for analysis. The concentration of the nitrate ester was thus determined directly and the sulphate ester was obtained by difference from the total 2,4-dinitrobenzyl alcohol consumed. Analyses of reaction mixtures showed that the rates of *O*-nitration were too fast for measurement even at 0° in 70% sulphuric acid and at lower acidities than this the yield of nitrate ester was negligible unless the nitric acid was present in considerable excess over the alcohol. Results at 0° for the range 55—93% sulphuric acid are given in Table 1. These show that with equimolecular initial concentrations of the alcohol and nitric acid in the more concentrated sulphuric acids the nitrate ester is initially formed much more rapidly than the sulphate ester but the latter is finally in large excess in the equilibrium mixture. The nitronium ion is clearly much more reactive than the sulphating entity but the *O*-nitration is reversed as the alcohol is gradually solvolysed; in addition, there may be direct conversion of the nitrate into sulphate ester. Attempts to follow the rate of hydrolysis of the nitrate failed because of the considerable time required for dissolution of the ester in all media except the most strongly acidic where reaction was too fast for measurement. The few analyses of mixtures obtained by starting with nitrate ester are included in Table 1 and they confirm the ultimate predominance of the sulphate ester.

The result of these investigations suggested that a larger proportion of nitrate ester might result even in the stronger acids if a higher initial concentration of nitric acid relative to the alcohol was used for all experiments at 25°; therefore a threefold excess of nitric acid was used. The composition of these equilibrium mixtures are expressed in terms of the equilibrium constants K_N and K_S for nitration and sulphation respectively. K_S, as

[1] Part I, preceding paper.
[2] Boschan, Merrow, and van Dolah, *Chem. Rev.*, 1955, **55**, 485.
[3] Farmer, *J. Soc. Chem. Ind.*, 1931, **50**, 75T; Chedin, Tribot, and Feneant, *Mém. Services chim. État*, 1948, **34**, 277; Rinkenbach and Aaronson, *Ind. Eng. Chem.*, 1931, **23**, 160; Aubertin, *Mém. Poudres*, 1948, **30**, 7; Ohman, *Svensk. kem. Tidskr.*, 1944, **56**, 328.
[4] Williams and Clark, (*a*) *J.*, 1956, 1304; (*b*) *J.*, 1957, 4218.

TABLE 1. *O-Nitration and sulphation of 2,4-dinitrobenzyl alcohol at 0°.*

$\%H_2SO_4$	$[HNO_3]$ (M)	[Alcohol] (M)	[Nitrate ester] (M)	Time (min.)	Nitrate ester (%)	Sulphate ester (%)
93	0·1	0·1	—	7	3·7	86
				240	4·1	85
87	0·1	0·1	—	6	19	43
				180	4	80
73	0·1	0·1	—	7	7	3
				240	8	8
70	0·1	0·1	—	7	6	1
				240	5	4
65	0·1	0·1	—	7	0	0
				240	2	0
65	2·0	0·08	—	4	2	—
				30	17	—
				120	17	—
65	4·0	0·1	—	45	55	—
				75	60	—
55	4·0	0·1	—	20	23	—
				35	34	—
				50	43	—
87	—	—	0·1	6	10	74
				180	9	78
77	—	—	0·1	100	9·7	18
75	—	—	0·1	210	5·6	25

previously defined,[4] is represented by (1) and K_N by (2), in which the bracketed quantities represent the experimentally determined concentrations at equilibrium. The constancy

$$K_S = [RSO_4]/[ROH] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$K_N = [RO{\cdot}NO_2]/[ROH][HNO_3] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

during several hours of the equilibrium composition once attained and the reproducibility of the analytical measurements are shown by the typical set of results for two duplicated experiments recorded in Table 2*a*. Errors in the alcohol and nitrate determinations are magnified in calculating K, but the largest difference between duplicate values of the latter is not more than 5%. Results for the range 75—85% sulphuric acid at 25° are given in Table 2*b*. The falling K_S and K_N values with decreasing acidity reflect the lower yields

TABLE 2. *O-Nitration and sulphation of 2,4-dinitrobenzyl alcohol at 25°.*

(*a*) Analyses of equilibrium mixtures in duplicate experiments in 80·7% H_2SO_3.

Initial concns.: [Alcohol] = 0·100M; $[HNO_3]$ = 0·318M.

Time (hr.)	10^2 [Alcohol] (M)		10^2 [Nitrate ester] (M)		10^2 [Sulphate ester] (M)		K_N		K_S	
	A	*B*	*A*	*B*	*A*	*B*	*A*	*B*	*A*	*B*
1	4·00	4·07	2·03	2·01	3·97	3·92	1·71	1·66	0·99	0·96
2	4·07	4·10	2·01	2·02	3·92	3·88	1·66	1·66	0·96	0·95
3	4·11	4·11	2·05	2·01	3·84	3·88	1·68	1·64	0·94	0·95
4	4·03	4·03	2·01	2·04	3·96	3·93	1·67	1·76	0·98	0·97

K_N (mean) = 1·67; K_S (mean) = 0·96.

(*b*) Variation of K_N and K_S with composition of the medium. Initial concns.: [Alcohol] = 0·100M; $[HNO_3]$ = 0·300M.

$H_2SO_4\%$	84·9	82·5	80·7	78·6	76·8	74·6
K_N	2·87	2·08	1·67	1·23	0·95	0·71
K_S	2·22	1·41	0·96	0·76	0·55	0·46
$\log K_N - H_0 + C_0$	−7·39	−7·23	−7·13	−7·10	−6·92	−6·75

of both esters. The variation of K_S with composition of the medium in fact is in excellent accord with that obtained in the same range of media in the absence of nitric acid by Williams and Clark.[4]

Acid Hydrolysis of Nitrate Ester.—It is reasonable to assume that in either reverse reaction, the hydrolysis of the ester if it could be measured directly would be of the first

order with respect to the ester. If, for nitration, the rate constants of the esterification reaction and the hydrolysis are k_2 and k_1 respectively, then at equilibrium

$$k_2[\mathrm{ROH}][\mathrm{HNO_3}] = k_1[\mathrm{RO{\cdot}NO_2}] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

and hence

$$k_1 = k_2/K_N \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

It was possible to measure K_N only for 2,4-dinitrobenzyl alcohol in these media and not k_2. For isopentyl alcohol however rates of esterification were measurable at 25° both in sulphuric acid and in perchloric acid solutions.[1] Isopentyl nitrate, like 2,4-dinitrobenzyl nitrate, dissolved too slowly in media in which rates of hydrolysis would have been measurable, and k_1 could not be determined directly. Calculated values of k_1 were however obtained from eqn. (4) and are recorded in Table 3. In the strongest acid employed, 75%

TABLE 3. *O-Nitration of isopentyl alcohol (k_2) and hydrolysis of isopentyl nitrate (k_1) at 25°.*

(*a*) In perchloric acid

$HClO_4$%	10^3k_2	K_N	$k_1 = k_2/K_N$	$\log K_N - H_0 - \log([Z^+]/[ZOH])$
62·0	157	10·0	0·157	4·29
60·8	71	7·39	0·096	4·27
59·3	27	5·93	0·0457	4·33
58·0	10·1	4·10	0·0246	4·31
56·3	5·0	3·24	0·0155	4·39
55·2	2·23	2·43	0·0092	4·38

(*b*) In sulphuric acid

H_2SO_4%	10^3k_2	K_N	$k_1 = k_2/K_N$	$\log K_N - H_0 + C_0$
67·0	31·5	19·5	0·0162	−4·28
66·0	25·2	22·4	0·0113	−4·07
65·3	21·9	20·2	0·0108	−4·01
63·5	9·4	13·5	0·0070	−3·97
62·4	5·04	8·3	0·0061	−4·00
60·0	1·72	5·6	0·0031	−3·87
57·7	0·73	3·71	0·0020	−3·73

sulphuric acid, equilibrium was attained in 15 minutes and during this time sulphation of isopentyl alcohol is negligible.

The calculated values of k_1 show that in both sulphuric and perchloric acid the rate of hydrolysis of isopentyl nitrate increased with acidity but only about half as rapidly as the forward esterification. Since the rate constant of esterification shows an approximate parallelism [4] with the acidity function, C_0, which increases about twice as rapidly as the Hammett acidity function, H_0, with increasing acid strength of the medium the possibility of a direct dependence of the hydrolysis rate constant on H_0 was evident. This was tested by plotting values of log k_1 at 25° against H_0 for both acids. Fig. 1 shows that reasonably good straight-line plots are obtained; the gradients of −0·92 for perchloric acid and of −0·85 for sulphuric acid are sufficiently close to unity to suggest that hydrolysis proceeds through the protonated nitrate ester formed in fractionally small amount.[5] This result also implies that the transition state involves only the protonated ester and does not include a molecule of water.[6] Protonation of a nitrate ester followed by release of a nitronium (nitryl) ion appears to occur in the concentrated acid since such solutions are nitrating media and in pure sulphuric acid there is cryoscopic evidence [7] of the production of five entities per molecule of added nitrate ester which can be represented by equations (5) and (6).

$$\mathrm{RO{\cdot}NO_2} + \mathrm{H_2SO_4} \rightleftharpoons \mathrm{ROH} + \mathrm{NO_2^+} + \mathrm{HSO_4^-} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

$$\mathrm{ROH} + 2\mathrm{H_2SO_4} \rightleftharpoons \mathrm{RO{\cdot}SO_2H} + \mathrm{H_3O^+} + \mathrm{HSO_4^-} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

[5] Hammett and Deyrup, *J. Amer. Chem. Soc.*, 1932, **54**, 2721.
[6] Zucker and Hammett, *ibid.*, 1939, **61**, 2779, 2785; Long and Paul, *Chem. Rev.*, 1957, **57**, 935.
[7] Kuhn, *J. Amer. Chem. Soc.*, 1947, **69**, 1974.

In aqueous ethanol it has been reported that the hydrolysis of nitrate esters is not catalysed by acids [8] and this is attributed to the loss of resonance stabilisation which would result from protonation of the nitrate group. The hydrolysis of methyl nitrate in aqueous solution also proceeds without any detectable catalysis by the nitric acid formed.[9] However in strongly acidic solutions the existence of a small fraction of the nitrate ester in the form of its conjugate acid is feasible and the extent of conversion into this form would increase with the acidity. The lower stability resulting from loss of resonance stabilisation would be relieved by the loss of a nitronium ion.

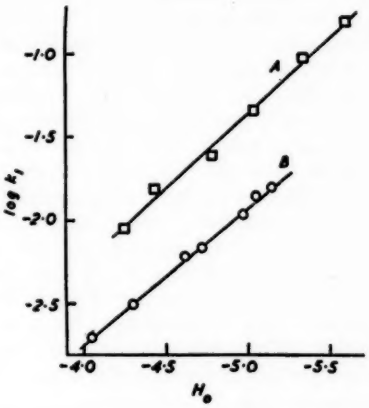


FIG. 1. *A*, $HClO_4$. *B*, H_2SO_4.

Dependence of K_N on the Acidity of the Media.—From the mechanisms which have been deduced for the esterification [1] and the hydrolysis, the equilibrium set up in strongly acidic media between an alcohol and its nitrate ester can be represented by eqn. (7):

$$ROH + NO_2^+ \rightleftharpoons RO{\cdot}NO_2 + H^+ \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

If K_0 represents the thermodynamic equilibrium constant, then by combining eqns. (7) and (2) we have

$$K_0/K_N = [HNO_3](H^+]f_{RONO_2}/[NO_2^+]f_{ROH}f_{NO_2^+} \quad . \quad . \quad . \quad . \quad . \quad (8)$$

where square brackets represent concentrations, parentheses activities, and f activity coefficients. Taking logarithms and combining this with eqn. (9) [5] and (10),[10]

$$H_0 = -\log (H^+)f_B/f_{BH^+} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

$$pK_{HNO_3} - pK_{ZOH} = \log ([NO_2^+]/[HNO_3]) - \log ([Z^+]/[ZOH]) \quad . \quad . \quad (10)$$

where B represents a Hammett-type base and ZOH a triphenylmethanol-type compound, we can derive (11):

$$\log K_N - H_0 - \log ([Z^+]/[ZOH]) = \Sigma pK - \Sigma \log f \quad . \quad . \quad . \quad . \quad (11)$$

where $$\Sigma pK = pK_{HNO_3} - pK_{ZOH} - pK_0$$

and $$\Sigma \log f = \log (f_{RONO_2}f_{BH^+}/f_{ROH}f_Bf_{NO_2^+})$$

If the log f term is not subject to considerable change over short ranges of media, the left-hand side of eqn. (11) should show some evidence of constancy. For perchloric acid,

[8] Baker and Neale, *J.*, 1955, 608.
[9] McKinley, McGee, and Moelwyn-Hughes, *Trans. Faraday Soc.*, 1952, **48**, 247.
[10] Murray and Williams, *J.*, 1950, 3322.

use of log ([Z^+]/[ZOH]) values for the indicator methyl 4-trimethylammoniumtriphenylmethyl ether perchlorate [1] makes the expected constancy quite evident, the sum of the three terms over the range 55—62% perchloric acid being 4·33 ± 0·06. For sulphuric acid, values of C_0 were used in place of the term log ([Z^+]/[ZOH]) since by definition [11] these terms only differ by the constant pK_{ZOH}; when eqn. (11) is tested in this form it is apparent that constancy is attained over the range 62—66% sulphuric acid for isopentyl alcohol and, less definitely, over the range 79—82% sulphuric acid for 2,4-dinitrobenzyl alcohol (see Fig. 2), although these ranges are considerably narrower than in perchloric acid (they correspond to *ca.* 0·5H_0 unit for both sulphuric acid ranges compared with the 1·3H_0 units for perchloric acid).

Previous discussion [1] has indicated that this difference in the two solvents is probably due to a greater diversity in the variation of activity coefficient ratios with composition of the medium in sulphuric acid. It would be useful to extend these studies to other alcohols to see if greater accord between the behaviour of the two solvents is possible in other ranges of media. For this purpose it would suffice to determine the equilibrium composition since eqn. (11) only requires evaluation of K_N and not of individual rate constants; the rapidity with which equilibrium is established is unimportant. In addition, the concurrent sulphation in sulphuric acid does not present any problem provided that analyses can be carried out as in the case of 2,4-dinitrobenzyl alcohol.

In the related equilibria set up when guanidines are nitrated or nitroguanidines denitrated in aqueous strong acids,[12] a direct dependence of the equilibrium constant K on the activity of water present has been found on the assumption that water participates in the equilibrium. The relationship is tested by a plot of log K against log (H_2O) which should give a straight line of negative unit slope. This has not been found to apply to the esterification reported here.

It has been assumed in this discussion that if any protonation of isopentyl alcohol or dinitrobenzyl alcohol occurs in the range of media investigated, this is limited for both compounds to a small amount. The arguments in favour of this view have already been considered for 2,4-dinitrobenzyl alcohol [4] and undoubtedly would apply to isopentyl alcohol. Any extensive change of protonation of either alcohol with increasing acidity in the ranges of media studied would have been revealed in the kinetic analysis.

Experimental

Materials and Media.—The preparation and standardisation of acids and the procedures used for isopentyl alcohol and nitrate have been described.[1] 2,4-Dinitrobenzyl alcohol was prepared [13] from 2,4-dinitrobenzyl chloride by conversion into acetate and hydrolysis of this with 50% sulphuric acid at 120°. The product, crystallised successively from water (with charcoal present), methanol, and benzene, had m. p. 115—116°. 2,4-Dinitrobenzyl nitrate was obtained in excellent yield by the action of freshly prepared anhydrous nitric acid on the alcohol. 15 g. of anhydrous nitric acid were added slowly to 5 g. of 2,4-dinitrobenzyl alcohol with shaking at 0°. After a few minutes, the solution was poured on ice and the yellow oil which separated was allowed to solidify. Recrystallisation gave 4·5 g. (70% yield) of 2,4-dinitrobenzyl nitrate, m. p. 39·5°.

Analysis of Reaction Mixtures.—The residual 2,4-dinitrobenzyl alcohol was determined by oxidation with dichromate in 6N-sulphuric acid by Williams and Clark's [3] method; neither nitric acid nor 2,4-dinitrobenzyl nitrate interfered. In preliminary experiments to find the relative extent of nitration and sulphation, the residual nitric acid was determined by the standard method [14] of reduction with excess of ferrous ammonium sulphate and back-titration

[11] Deno, Jaruzelski, and Schriesheim, *J. Amer. Chem. Soc.*, 1955, **77**, 3044.
[12] Simkins and Williams, *J.*, 1952, 3086; Hardy-Klein, *J.*, 1957, 70.
[13] Friedländer and Cohn, *Monatsh.*, 1902, **23**, 546; *Ber.*, 1902, **35**, 1266.
[14] Kolthoff, Sandell, and Mostovitz, *J. Amer. Chem. Soc.*, 1933, **55**, 1454; Lowen and Williams, *J.*, 1950, 3312.

with dichromate; the nitrate ester which would have interfered in this determination was first removed by extraction with carbon tetrachloride. In the experiments in which the presence of excess of nitric acid made this method unsuitable, the carbon tetrachloride extract of nitrate ester was evaporated to dryness and the residual oil dissolved in concentrated sulphuric acid and analysed for nitrate by direct titration with ferrous sulphate solution.[15]

Evaluation of Equilibrium Constants.—For the precise determination of the composition of equilibrium mixtures formed by 2,4-dinitrobenzyl alcohol and nitric acid at 25° a new absorp-

FIG. 2. *A, 2,4-Dinitrobenzyl alcohol; B, Isopentyl alcohol.*

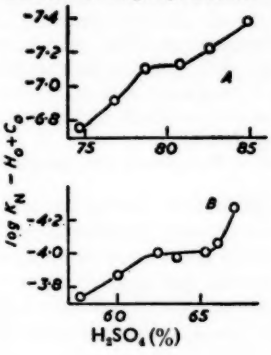
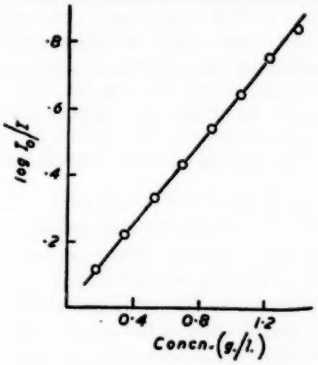


FIG. 3. *2,4-Dinitrobenzyl alcohol.*



tiometric method was devised for the direct determination of 2,4-dinitrobenzyl nitrate. A 2 ml. sample of the equilibrium mixture was diluted to 6N-sulphuric acid and after oxidation of the unchanged alcohol with dichromate the solution was extracted twice with 10 ml. portions of benzene; this extraction removed both the nitrate ester and the oxidation product, 2,4-dinitrobenzoic acid. The latter was removed by washing the combined benzene extracts twice with 5 ml. portions of 0·2N-sodium hydroxide, and once with water, and then filtering into a 25 ml. flask and making up to the mark with benzene. The absorption of this solution was measured on a Spekker photoelectric absorptiometer having 1 cm. cells with H 556 filters, which give a high transmission of ultraviolet light. The concentration of nitrate ester were obtained from a standard curve previously prepared by using a series of solutions of known concentration in benzene (see Fig. 3). By this method, alcohol and nitrate ester determinations were carried out on the same sample of the equilibrium mixture; for each experiment, samples were removed at four half-hourly or hourly intervals to confirm that a true equilibrium had been established.

ROYAL HOLLOWAY COLLEGE, ENGLEFIELD GREEN, SURREY. [*Received, May 8th*, 1959.]

[15] Treadwell and Vontobel, *Helv. Chim. Acta*, 1937, **20**, 573.

786. *Nitration of Alcohols at Oxygen Centres. Part III.*[1] *The Reaction of Nitric Acid and 2,4-Dinitrobenzyl Alcohol in Acetic Anhydride–Acetic Acid Solvent.*

By T. G. Bonner.

The rate of conversion of 2,4-dinitrobenzyl alcohol into its nitrate ester by nitric acid in several acetic anhydride–acetic acid mixtures has been measured. The *O*-nitration proceeds to completion and no acetylation of the alcohol is apparent. The reaction is of the second order with respect to the nitric acid, which suggests that dinitrogen pentoxide formed in fractionally small amount is the active nitrating agent. Within the range of media containing 0—10% of acetic anhydride a maximum rate of reaction appears at about 7% acetic anhydride although at a much higher acetic anhydride content the reaction is immeasurably fast.

The various equilibria which may be present in the system are discussed.

The nitrating property of nitric acid in acetic anhydride first demonstrated by Orton[2] in the nitration of aromatic compounds was until fairly recently assumed to be due to the presence of acetyl nitrate, since preparations of this reagent showed similar nitrating behaviour.[3] A kinetic study[4] of the nitration of benzene by benzoyl nitrate in carbon tetrachloride however has established that in the case of this mixed anhydride a small stationary concentration of the more reactive dinitrogen pentoxide is formed in equilibrium with benzoic anhydride according to eqn. (1), and that the *C*-nitration proceeds solely by

$$2BzO{\cdot}NO_2 \rightleftharpoons N_2O_5 + Bz_2O \quad \ldots\ldots\ldots\ldots \quad (1)$$

attack of the dinitrogen pentoxide and not to any detectable extent directly by benzoyl nitrate. The same report suggests that a similar mechanism is operative in the nitration of benzene by nitric acid and acetic anhydride in carbon tetrachloride[5] and includes the qualitative observation that there is an optimum amount of acetic anhydride, excess of which decreases the rate of nitration by reversing the equilibrium in which the dinitrogen pentoxide is formed.

In the conversion of alcohols into nitrate esters, nitric acid in a mixed solvent of acetic anhydride and acetic acid is frequently used as the nitrating medium.[3,6] The experience gained with 2,4-dinitrobenzyl alcohol in *O*-nitration studies in other media[1] made it possible to investigate whether dinitrogen pentoxide was the essential intermediate in promoting *O*-nitration in acetic anhydride–acetic acid. In this reaction, apart from the problem of the nitrating entity, there is the possibility of a competing acetylation.

Preliminary examination of the interaction of nitric acid with 2,4-dinitrobenzyl alcohol in this system showed that a 90% yield of the nitrate ester was readily attained, and that as a preparative method this procedure was superior to that of using a mixture of nitric acid and sulphuric acid. The method of analysing reaction mixtures of 2,4-dinitrobenzyl alcohol in the latter solvent[1] by quantitative oxidation of the alcohol with acidic dichromate and spectrophotometric determination of the nitrate ester after extraction with benzene was found to be applicable to the acetic anhydride–acetic acid solutions without modification. Some preliminary analyses were carried out in a medium containing about 4% of acetic anhydride in acetic acid to establish whether the amount of nitrate ester formed after different times corresponded to the amount of alcohol consumed. A typical result

[1] Part II, Bonner and Frizel, preceding paper.
[2] Orton, *J.*, 1902, 806.
[3] Pictet and Khotinsky, *Compt. rend.*, 1907, **144**, 210; *Ber.*, 1907, **40**, 1164.
[4] Gold, Hughes, and Ingold, *J.*, 1950, 2467.
[5] Cohen and Wibaut, *Rec. Trav. chim.*, 1935, **54**, 409.
[6] Boschan, Merrow, and Van Dolah, *Chem. Rev.*, 1955, **55**, 485.

with initial concentrations of *ca.* 0·1M-2,4-dinitrobenzyl alcohol and 0·3M-nitric acid is shown in Table 1. The constancy to within 2% of the sum of the independently determined concentrations of the alcohol and nitrate excludes the possibility that any acetate

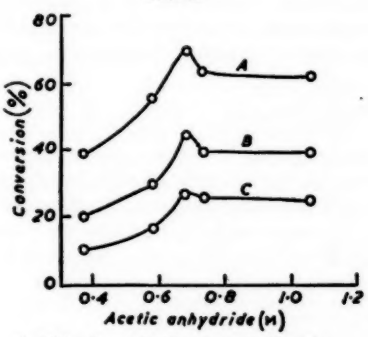
TABLE 1. *Analysis of an O-nitration reaction mixture at 25° in acetic acid containing 0·39M-acetic anhydride.*

Initial concns.: [ROH] = 0·1020M; [HNO_3] = 0·3212M.

Time (min.)	0	5	10	15	30	60	90	120	150
10^2[ROH] (*A*).....	10·20	9·42	8·58	7·87	6·28	4·35	3·05	2·33	1·88
10^2[RO·NO_2](*B*)...	0	1·06	1·75	2·48	4·01	6·02	6·99	7·82	8·23
A + *B*	10·20	10·48	10·33	10·35	10·29	10·37	10·04	10·15	10·11

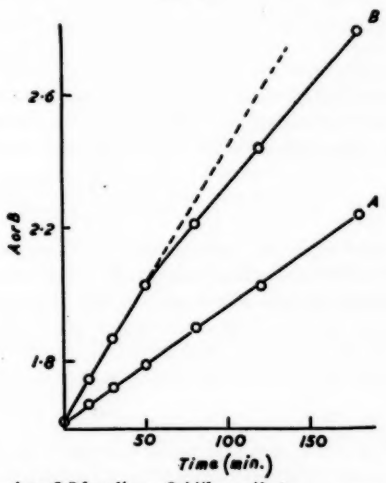
ester is separately formed in detectable amount concurrently with the nitrate ester. This is in agreement with the failure to detect any acylated product in the nitration of anisole

FIG. 1.



A, 100 min.; *B*, 40 min.; *C*, 20 min.

FIG. 2.



$A = 2{\cdot}3 \log \{(a - 2x)/(b - x)\} + 2x(2b - a)/a(a - 2x).$

$B = 2{\cdot}3 \log \{(a - x)(b - x)\} - x(a - b)/a(a - x).$

with acyl nitrates in acetonitrile.[7] It is clearly unlikely that the acetate ester has the alternative rôle of a highly reactive intermediate. Experiments to confirm this point showed that over several hours (a period much longer than that required for the completion of the *O*-nitration of the alcohol) added acetate ester was not noticeably attacked by nitric acid in the acetic anhydride–acetic acid solvent, the final analysis showing that at least 96% of the acetate ester remained unchanged.

Variation of Rate of O-Nitration with Acetic Anhydride Concentration.—Measurements of the extent of conversion of 2,4-dinitrobenzyl alcohol into its nitrate ester in a given time showed that the presence of acetic anhydride was essential for reaction, no change being observed when nitric acid alone was present in the acetic acid solvent. Over the range 0—10% (*i.e.*, 0—1M) acetic anhydride there was an increasing rate of conversion into the nitrate ester with increasing acetic anhydride concentration, a maximum rate appearing in the medium containing 7% of acetic anhydride. This is shown in Fig. 1 in which the percentage conversions of 2,4-dinitrobenzyl alcohol into nitrate ester at three separate time intervals for five different acetic anhydride–acetic acid solvents are plotted against

[7] Burton and Praill, *J.*, 1955, 729.

molarity of acetic anhydride. Although the maximum is clearly evident from the curves, there is only a slight fall in rate from this point to that corresponding to a medium containing 10% of acetic anhydride. Rates of reaction at much higher acetic anhydride concentrations, *e.g.*, 40%, were too fast for measurement so that in the range 10—40% an increase in rate with acetic anhydride content reappears. By means of Fig. 1, the maximum obtained at 7% of acetic anhydride is made evident without knowledge of the mechanism of the reaction. It is also evident that, if the *O*-nitration proceeds exclusively through the action of dinitrogen pentoxide formed by dehydration of the nitric acid and regulated by an equilibrium similar to (1), other equilibria will be necessary to maintain an effective constancy in the fraction of nitric acid converted into dinitrogen pentoxide in media containing acetic anhydride concentrations from 0·7 to 1·06M. An indication of the equilibria set up in these systems has been provided by reports of studies of the physical properties of various mixtures of nitric acid, dinitrogen pentoxide, acetic anhydride, and acetic acid. Vapour-pressure measurements on nitric acid–acetic anhydride mixtures [8] show a maximum near the 1 : 1 mole mixture corresponding to substantially complete formation of acetyl nitrate according to eqn. (2). With increasing nitric acid content

$$Ac_2O + HNO_3 \rightleftharpoons AcO{\cdot}NO_2 + AcOH \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

above the 1 : 1 mole mixture, the vapour pressure rises to a maximum at a mole fraction of 0·84 corresponding to formation of dinitrogen pentoxide which can be represented by either equation (3) or (4). Further increase in the nitric acid content decreases the vapour

$$AcO{\cdot}NO_2 + HNO_3 \rightleftharpoons AcOH + N_2O_5 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

$$Ac_2O + 2HNO_3 \rightleftharpoons N_2O_5 + 2AcOH \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

pressure until that corresponding to pure nitric acid is finally attained. Raman spectra [9] confirm that, when acetic anhydride is in excess over nitric acid, there is complete conversion of nitric acid into acetyl nitrate and, when nitric acid is in large excess, *i.e.*, >80 moles %, dinitrogen pentoxide is the major product and only traces of acetyl nitrate are present. The formation of acetyl nitrate from nitric acid is represented as the dehydration (4) followed by reaction (5) which is complete when the acetic anhydride is in excess. Mix-

$$N_2O_5 + Ac_2O \rightleftharpoons 2AcO{\cdot}NO_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

tures of nitric acid and acetic anhydride in the mole ratio 2 : 1 and of dinitrogen pentoxide and acetic acid with mole ratio 1 : 2 gave the same spectra, confirming the rapid establishment of the equilibrium (4). The ultraviolet spectra of the system dinitrogen pentoxide–acetic anhydride [10] indicated some instability over the range 12—96%; for nitric acid–acetic anhydride mixtures containing more than 96% of nitric acid, the ultraviolet spectra resembled those of high concentrations of dinitrogen pentoxide in nitric acid, while mixtures containing less than 7% of nitric acid had a spectra similar to those of solutions of low concentration of dinitrogen pentoxide in nitric acid. Although these results led Jones and Thorn to suggest that in both cases, *i.e.*, of high and low nitric acid concentrations in acetic anhydride, the operative equilibrium was (4) lying well to the right, their results do not exclude the possibility that acetyl nitrate may be substantially formed at the lower nitric acid concentration. More recently, measurements of the density, viscosity, and refractive index [11] of the systems acetic anhydride–nitric acid and acetic acid–nitric acid have also shown that a 1 : 1 molar mixture of acetic anhydride and nitric acid gives almost complete conversion into acetyl nitrate according to eqn. (2) and that appreciable amounts of dinitrogen pentoxide are only formed according to (4) when the concentration of nitric acid is very high. The conclusion was also reached that acetyl nitrate is not likely to be an intermediate in the formation of dinitrogen pentoxide.

[8] Vandoni and Viala, *Mém. services. chim. État*, 1945, **32**, 80.
[9] Chedin and Feneant, *Compt. rend.*, 1949, **229**, 115—117.
[10] Jones and Thorn, *Canad. J. Res.*, 1949, **27***B*, 580—603.
[11] Malkova, *J. Gen. Chem. U.S.S.R.*, 1954, **24**, 1151 (U.S. translation).

The Kinetic Order of the O*-Nitration in the Acetic Anhydride–Acetic Acid Solvent.*— Before any use could be made of the above data, it was necessary to determine the kinetic order of the *O*-nitration. Some preliminary experiments were carried out with a solvent containing 0·37M-acetic anhydride in acetic acid, using a fixed initial concentration of 0·04M-2,4-dinitrobenzyl alcohol (*b*) for all runs, and systematically increasing the initial nitric acid concentration (*a*) from 0·2 to 0·8M. Higher concentrations of nitric acid appeared to result in some side reactions to give easily oxidisable products which interfered in the method of analysis. The results, although accurately reproducible for duplicate runs, did not satisfy the rate equation for a second-order reaction (*i.e.*, first-order with respect to the alcohol and to the nitric acid), the plots of log $(a - x)/(b - x)$ against time in all cases giving a smooth curve. For reactions in which the nitric acid concentration was in tenfold or greater excess over the alcohol the results were plotted as for a first-order reaction of the alcohol only. Although there was an evident curvature when log $(b - x)$ was plotted against time, rate constants could be calculated from the straight portion of the curve covering up to about 25% conversion of the alcohol into nitrate ester. The significant feature then appeared that the ratio of the rate constant to the square of the initial nitric acid concentration was a constant independent of the latter. The reaction was therefore of the second order with respect to the nitric acid. These results suggested that *O*-nitration did not take place through attack by acetyl nitrate on the alcohol since this would most probably require first-order dependence on the nitric acid. To derive the simplest kinetic equation on the basis of a reaction of the first order with respect to the alcohol and second order with respect to the nitric acid, it was assumed that the two molecules of nitric acid were initially involved in the formation of dinitrogen pentoxide which then reacted with the alcohol.

Stoicheiometrically, in this reaction a molecule of nitric acid is liberated for each molecule of alcohol consumed, and if the reactions are represented as in (6) with the concentrations of the reactants at time *t* as shown, the rate equation can be represented

$$\underset{a-2x}{2HNO_3} \longrightarrow N_2O_5;\ \underset{b-x}{ROH} + N_2O_5 \longrightarrow \underset{x}{RO{\cdot}NO_2} + \underset{x}{HNO_3} \quad . \quad . \quad . \quad . \quad . \quad (6)$$

by eqn. (7) from which the kinetic equation (8) is derived:

$$dx/dt = k(a - x)^2(b - x) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

$$k(a - b)^2t = 2{\cdot}3 \log \{b(a - x)/a(b - x)\} - (a - b)/a(a - x) \quad . \quad . \quad (8)$$

If however the nitric acid liberated in the *O*-nitration is removed, *e.g.*, by conversion into acetyl nitrate as in eqn. (2), the rate equation then becomes that shown in (9) and the derived kinetic equation is (10):

$$dx/dt = k(a - 2x)^2(b - x) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

$$kt(a - 2b)^2 = 2{\cdot}3 \log \{b(a - 2x)/a(b - x)\} + 2x(2b - a)/a(a - 2x) \quad . \quad (10)$$

With a fixed initial concentration of 2,4-dinitrobenzyl alcohol of 0·04M and with that of the nitric acid within the range 0·2—0·8M, it was found in all cases that the kinetic equation (10) was obeyed. This is demonstrated in Fig. 2 in which the plot of $2{\cdot}3 \log \{(a - 2x)/(b - x)\} + 2x(2b - a)/a(a - 2x)$ against *t* (eqn. 10) is a straight line over the 70% change followed in the reaction while the plot of $2{\cdot}3 \log \{(a - x)/(b - x)\} - x(a - b)/a(a - x)$ (eqn. 8) against *t* deviates markedly from a straight line. With the reactant concentrations indicated, a constant value of *k* is obtained from these plots for kinetic measurements in a given medium, as the results shown in Table 2 for the medium containing 0·37M-acetic anhydride demonstrate. The rate constants obtained from eqn. (10) over the range of media investigated show that there is an optimum acetic anhydride concentration at about 0·7M, as mentioned previously. When the initial concentration of the alcohol is altered, the kinetic equation (10) is still obeyed but the value of the rate constant changes slightly. The effect is small in the 0·37M-medium (experiments 44 and

45) but is more marked in media with a higher acetic anhydride content; a more detailed investigation is necessary to interpret this feature.

Evidently there is more than one reaction scheme which satisfies the kinetic order

TABLE 2. *Rate constants of O-nitration of 2,4-dinitrobenzyl alcohol in acetic anhydride–acetic acid.* (*Initial concns. shown.*)

Expt.	$[Ac_2O]$ (M)	10^3[ROH] (M)	$10^3[HNO_3]$ (M)	k	Expt.	$[Ac_2O]$ (M)	10^3[ROH] (M)	$10^3[HNO_3]$ (M)	k
41	0·37	4·06	16·37	0·22	29	0·58	4·13	20·45	0·46
43	,,	4·07	16·26	0·20	30	,,	4·09	15·33	0·46
49	,,	4·06	20·48	0·22					
48	,,	4·15	41·80	0·21	26	0·68	4·16	16·20	0·76
50	,,	4·16	40·95	0·21					
51	,,	4·14	63·30	0·22	22	0·73	4·14	21·15	0·67
52	,,	4·16	79·20	0·19	23	,,	4·18	15·86	0·71
44	,,	6·10	21·70	0·18	18	1·06	4·22	15·84	0·65
45	,,	2·13	22·00	0·17	63	,,	4·04	40·20	0·68

found experimentally and provides for dinitrogen pentoxide as the active nitrating agent. The main possibilities are shown in (i)—(iv):

(i) $Ac_2O + HNO_3 \rightleftharpoons AcO{\cdot}NO_2 + AcOH$ and either (ii), (iii), or (iv)
(ii) $2AcO{\cdot}NO_2 \rightleftharpoons Ac_2O + N_2O_5$
(iii) $AcO{\cdot}NO_2 + HNO_3 \rightleftharpoons AcOH + N_2O_5$
(iv) $Ac_2O + 2HNO_3 \rightleftharpoons 2AcOH + N_2O_5$

Since the nitration of benzene by pure dinitrogen pentoxide in carbon tetrachloride is immeasurably fast and rate measurements are only possible when deactivating substituents are present,[12] the easier *O*-nitration in acetic anhydride–acetic acid can proceed at a measurable rate only if the fraction of nitric acid present as dinitrogen pentoxide in this system is extremely small. Although reaction (ii) provides an obvious means of interpreting the occurrence of an optimum concentration of dinitrogen pentoxide, it does not account for the immeasurably fast rate at a much higher acetic anhydride concentration. This can be accommodated by reactions (iii) or (iv) since the lower relative amount of acetic acid in such media would correspond to a shift in equilibrium to the right in (iii) and (iv). Further, a large increase in the ratio of acetic anhydride to acetic acid in media containing a very low concentration of perchloric acid (<0·1M) leads to a considerable increase in the acidity of the medium;[13] this would enhance the formation of dinitrogen pentoxide in both cases.

EXPERIMENTAL

Materials and Media.—2,4-Dinitrobenzyl alcohol and its nitrate ester are described in the preceding paper.[1] " AnalaR " acetic acid was distilled to give a product of m. p. 16·5°. Acetic anhydride, distilled twice through a small fractionating column, was weighed in appropriate amount and made up to a known volume at 25° with the acetic acid; allowance was made for the small amount of water in the acetic acid in calculating the composition of each medium.

Kinetic Measurements.—It was established that the acetic anhydride–acetic acid solvent did not interfere with the methods of determination of 2,4-dinitrobenzyl alcohol (by dichromate oxidation) and of its nitrate ester (spectrophotometrically) previously described.[1] The alcohol was weighed into a B24 cap which fitted the neck of the reaction flask containing 20 ml. of the medium at 25°. The cap was inserted into the neck of the reaction flask at zero time and on vigorous shaking the alcohol dissolved almost instantaneously. The flask was returned to the thermostat at 25° and 2 ml. samples were removed at intervals and run into 10 ml. of a solution of 4 g. of potassium dichromate in 1 l. of 6N-sulphuric acid. Next morning the excess of dichromate was determined with potassium iodide and standard thiosulphate solution by

[12] Gold, Hughes, Ingold, and Williams, *J.*, 1950, 2452.
[13] MacKenzie and Winter, *Trans. Faraday Soc.*, 1948, **44**, 159.

the usual procedure. When the 2,4-dinitrobenzyl nitrate ester formed was determined simultaneously, the dichromate solutions after the overnight standing were extracted twice with 10 ml. portions of benzene. The extracts were combined, washed with 0·2N-sodium hydroxide, then with water, filtered into 25 ml. volumetric flasks, and made up to the mark with benzene washings.

Miss M. Pestell is thanked for experimental assistance.

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787. *The Chemical Action of Ionising Radiations in Solution. Part XXIII.* The Action of* ^{60}Co-*Gamma-rays on Aqueous Solutions of Ethanol in the Liquid and the Frozen State.*

By J. T. ALLAN, E. M. HAYON, and J. WEISS.

The action of ^{60}Co-gamma-rays on deaerated aqueous solutions of ethanol at different concentrations (from 10^{-3}—5M) was studied in the liquid and in the frozen state from 20° to −196°. The products were acetaldehyde, butane-2,3-diol, hydrogen peroxide, and molecular hydrogen. The dependence of the yields of these products on solute concentration, physical state, and temperature has been investigated in detail. A mechanism is put forward to account for the experimental results, with particular reference to the reactions in the frozen solutions.

THE chemical effects of ionising radiations in dilute aqueous solutions yield reactive species such as H and OH [1] and, to a smaller extent, so-called " molecular " products H_2 and H_2O_2 from water.[2] The effect of gamma-radiation on ice, in the presence and in the absence of oxygen, was recently investigated by Ghormley and Stewart.[3] They found the yields of H_2 and H_2O_2 in oxygenated systems to increase with increase in temperature, *e.g.*, $G(H_2O_2)$ increased from 0·2 to 0·7 and $G(H_2)$ from 0·1 to 0·25 between −200 and −15°. In earlier work on the effect of *X*-rays, γ-rays, and α-particles, the yields of H_2 and H_2O_2 at different temperatures of irradiation [4a] were found in all cases to decrease appreciably on going from water to ice, and generally to decrease with a decrease in temperature. Recent work [4b] on the tritium β-ray irradiation of water vapour has shown that the total yield from its decomposition is considerably greater than from the liquid.

It was thought, therefore, that irradiation of frozen aqueous solutions of an organic solute which is a good acceptor for the radiation-produced reactive species formed from the water, might be of interest particularly with regard to the extent of the total decomposition of water at various low temperatures. Ethanol was chosen as solute, as the radiation chemistry of its aqueous solutions has been investigated previously.[5]

At room temperature in absence of oxygen it gives mainly acetaldehyde and butane-2,3-diol; in presence of oxygen, glycol was not formed. We investigated the yields of the radiolysis products from −196° to 20°, and the dependence on the ethanol concentration.

RESULTS

Unless otherwise stated, the irradiations of aqueous ethanol were carried out in 0·1N-sulphuric acid *in vacuo*. The products from deaerated ethanol solutions were acetaldehyde, butane-2,3-diol, hydrogen peroxide and hydrogen. The diol, previously found in the liquid systems,

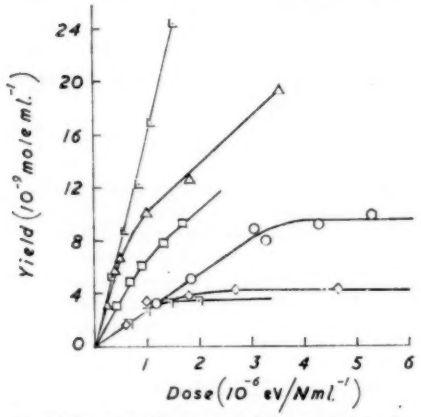
* Part XXII, *J.*, 1958, 2467.

[1] Weiss, *Nature*, 1944, **153**, 748.
[2] Allen, *Ann. Rev. Phys. Chem.*, 1952, **3**, 57.
[3] Ghormley and Stewart, *J. Amer. Chem. Soc.*, 1956, **78**, 2934.
[4] (*a*) Bonet-Maury and Lefort, *J. chim. Phys.*, 1950, **47**, 179; Lefort, in " Actions Chimiques et Biologiques des Radiations," Part II, Ed. M. Haissinsky, Masson et Cie, Paris, 1955, p. 203; (*b*) Firestone, *J. Amer. Chem. Soc.*, 1957, **79**, 5593.
[5] Jayson, Scholes, and Weiss, *J.*, 1957, 1358.

is also formed in the frozen solutions, but no quantitative measurements were made on the latter.

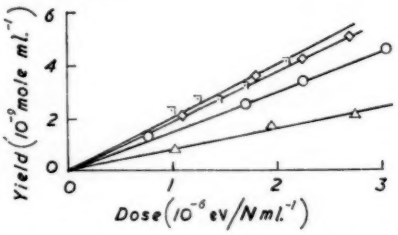
The lowest practicable doses were used to determine the *initial* yields. Fig. 1 shows several yield–dose plots for the formation of acetaldehyde from frozen ethanol solutions at −78° in

FIG. 1. *Yield–dose curves for the formation of acetaldehyde in the irradiation of deaerated aqueous solutions of ethanol* (pH = 1·2) *with* ^{60}Co-*gamma-rays at* −78°, *at different solute concentrations.*



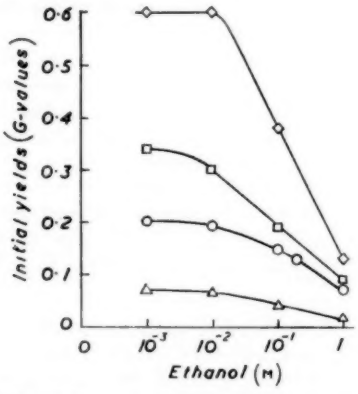
¬|, 10^{-3}M; ◇, 10^{-2}M; ○, 10^{-1}M; □, 5 × 10^{-1}M; △, 1M; ⌞, 5M-ethanol.

FIG. 2. *Yield–dose curves for the formation of hydrogen peroxide in the irradiation of deaerated aqueous solutions of ethanol* (pH = 1·2) *with* ^{60}Co-*gamma-rays at* −78° *at different solute concentrations.*



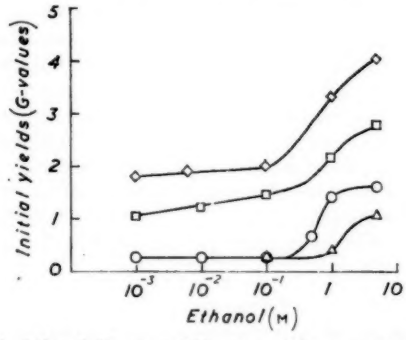
¬|, 10^{-3}M; ◇, 10^{-2}M; ○, 10^{-1}M; △, 1M-ethanol.

FIG. 3. *Dependence of the initial yields of hydrogen peroxide on the concentration of ethanol in deaerated aqueous solutions irradiated with* ^{60}Co-*gamma-rays at different temperatures* (pH = 1·2).



◇, 18° and 2°; □, −10°; ○, −78°; △, −196°.

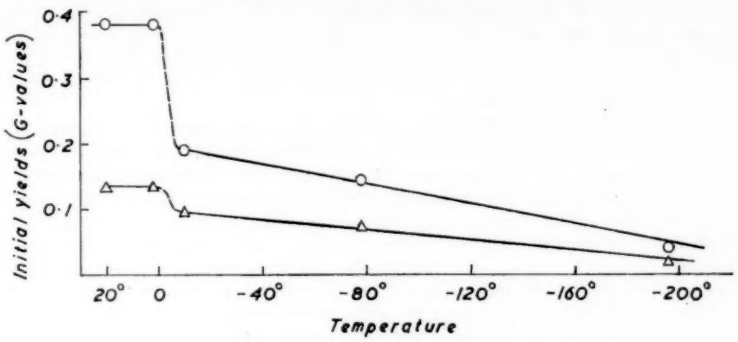
FIG. 4. *Dependence of the initial yields of acetaldehyde on the concentration of ethanol in deaerated aqueous solutions irradiated with* ^{60}Co-*gamma-rays at different temperatures* (pH = 1·2).



◇, 18° and 2°; □, −10°; ○, −78°; △, −196°.

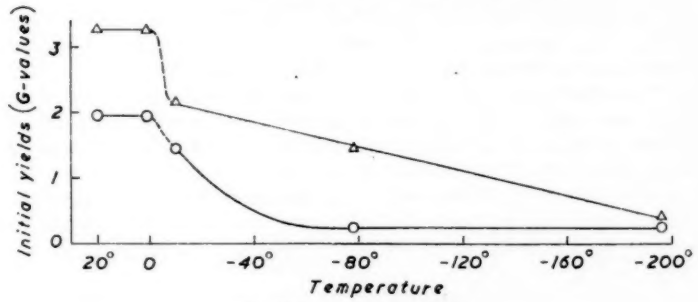
10^{-3}M—5·0M-ethanol. Fig. 2 shows similar yield–dose plots for the simultaneous formation of hydrogen peroxide. Fig. 1 shows that the *initial* yields of acetaldehyde are the same from 10^{-3} to 10^{-1}M-ethanol. Above 10^{-1}M-ethanol the yield of acetaldehyde increases with increasing solute concentration. On the other hand, the yields of H_2O_2 decrease with increase in solute concentration in the range of 10^{-3}—1·0M-ethanol (Fig. 2).

FIG. 5. *Temperature-dependence of the initial yields of hydrogen peroxide in deaerated aqueous solutions of ethanol irradiated with* ^{60}Co-*gamma-rays* (pH = 1·2).



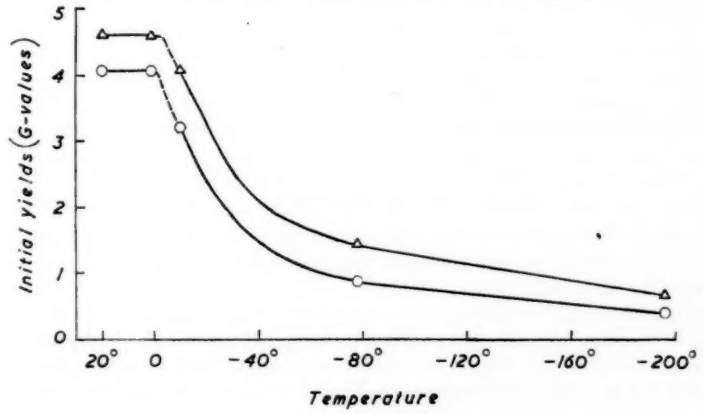
○, 10^{-1}M; △, 1M-ethanol.

FIG. 6. *Temperature-dependence of the initial yields of acetaldehyde in deaerated aqueous solutions of ethanol irradiated with* ^{60}Co-*gamma-rays* (pH = 1·2).



○, 10^{-1}M; △, 1M-ethanol.

FIG. 7. *Temperature-dependence of the initial yields of hydrogen in deaerated solutions of ethanol irradiated with* ^{60}Co-*gamma-rays* (pH = 1·2).



○, 10^{-1}M; △, 1M-ethanol.

Fig. 3 shows the variation of the *initial* yields of hydrogen peroxide with solute concentration in 10^{-3}—1·0M-ethanol and their dependence on temperature. Measurements were carried out at 20° and 2° and in the frozen state at −10°, −78°, and −196°. The yields of H_2O_2 decrease (i) with increase in solute concentration, (ii) in going from the liquid to the solid phase, and (iii) with decrease in temperature. Initial yields were all derived from yield–dose curves. The yield of hydrogen peroxide obtained on irradiation of deaerated dilute ethanol solutions at room temperature (20°) was $G = 0{\cdot}6$.

The dependence of the initial yields of acetaldehyde in the range 10^{-3}—5·0M-ethanol is given in Fig. 4, which also shows their dependence on temperature and state between 20° and −196°. It is noteworthy that at any one temperature there is only a slight concentration-dependence of the yield of acetaldehyde in the region 10^{-3}—10^{-1}M-ethanol: above 10^{-1}M the yields of acetaldehyde increase rapidly with increase in solute concentration, this increase taking place in the liquid as well as in the frozen solutions down to −196°. Fig. 5 shows the temperature-dependence of the yields of hydrogen peroxide in the irradiation of deaerated 0·1N-sulphuric acid solutions of 10^{-1}M- and 1·0M-ethanol. The abrupt decrease in the yields between the liquid and the frozen state, and particularly the almost linear decrease of hydrogen peroxide with decrease in temperature from −10° to −196°, is notable. Figs. 6 and 7 show the temperature-dependence of the yields of acetaldehyde and hydrogen, respectively, from irradiations of 10^{-1} and 1·0M-ethanol solutions.

Discussion

The physical processes following absorption of ionising radiation consist of excitations and ionisations. The formation of the " molecular " products H_2 and H_2O_2 is probably due to molecular interactions in the regions of dense energy release within the " clusters." Outside the " clusters " the excitations and ionisations will lead to H atoms and OH radicals which may react with any solute present. For present purposes, the various suggested species allied to H or OH radicals will be ignored. At sufficiently high solute concentrations, it is to be expected that the solute will compete with the interaction of the active species within the " clusters." The results in Fig. 3 indicate that the yields of " molecular " hydrogen peroxide obtained from irradiation of deaerated solutions of ethanol decrease with increase in solute concentration. The same effect was observed over the range from 2° to −196°.

The reaction of OH radicals with ethanol in aqueous solution is generally assumed to result in a dehydrogenation at the α-carbon atom:

$$CH_3{\cdot}CH_2{\cdot}OH + OH \longrightarrow CH_3{\cdot}\dot{C}H{\cdot}OH + H_2O \quad (1)$$

Hydrogen atoms, in air-free acidified solutions, dehydrogenate organic solutes at the α-carbon atom:

$$CH_3{\cdot}CH_2{\cdot}OH + H \longrightarrow CH_3{\cdot}\dot{C}H{\cdot}OH + H_2 \quad (2)$$

$$CH_3{\cdot}CH_2{\cdot}OH + H_2^+ \longrightarrow CH_3{\cdot}\dot{C}H{\cdot}OH + H_2 + H^+ \quad (3)$$

The formation of acetaldehyde and of butane-2,3-diol can be accounted for as follows:

$$2CH_3{\cdot}\dot{C}H{\cdot}OH \longrightarrow CH_3{\cdot}CHO + CH_3{\cdot}CH_2{\cdot}OH \quad (4)$$

$$2CH_3{\cdot}\dot{C}H{\cdot}OH \longrightarrow (CH_3{\cdot}CH{\cdot}OH)_2 \quad (5)$$

The question now arises as to whether the interpretation of the radiation-induced chemical effects in frozen systems involve the same reactive species and chemical reactions as have been assumed for the liquid phase.

Although lowering of the temperature may not alter very radically the primary radiation processes,[6] it is bound to affect the subsequent chemical reactions. In general, it may be difficult to give a straightforward interpretation of the radiation-induced reactions when the system is irradiated in the frozen state because, owing to the greatly reduced mobility

[6] Livingston, Zeldes, and Taylor, *Discuss. Faraday Soc.*, 1955, **19**, 166.

of the reactive intermediates and of all the other reactants in the solid state, most of the reactions subsequent to irradiation probably take place during the " thawing " and not in the frozen state at the lowest temperature during irradiation.

However, in a comparison of the liquid and solid systems, several other factors may also have to be taken into account, *e.g.*, the structure of the frozen solid at different temperatures and excitation and/or electron transfers in the solid state.

The above results show that the primary chemical processes are apparently considerably shortened as seen from a comparison of ice at −10° and water at 2°, and that the radiolysis is further reduced with decrease in temperature between −10° and −196°. The total decomposition of the water molecules can be calculated from the stoicheiometric relation:

$$G(H_2O) = 2G(H_2O_2) + G(OH) = 2G(H_2) + G(H) \quad . \quad . \quad . \quad (6)$$

Taking the yield of " molecular " hydrogen to be the yield of hydrogen found on irradiation of rapidly frozen oxygen-saturated water [3] and assuming that the yield of hydrogen found on irradiation of aqueous ethanol solutions (Fig. 7) to be the sum of the " molecular " hydrogen plus that formed by the dehydrogenation process [reactions (2) and (3)], one can calculate $G(-H_2O)$ from eqn. (6). The result is shown in columns 5 and 6 of Table 1.

TABLE 1. *G-Values for hydrogen and total water decomposition in frozen and liquid ethanol–water solutions and comparison with water.*

	Aqueous ethanol				
	EtOH = 0·1M		EtOH = 1·0M		Water
Temp.	$G(H_2)$	$G(-H_2O)$	$G(H_2)$	$G(-H_2O)$	$G(H_2)$
−200°	0·40	0·50	0·68	0·78	0·10 [a]
−78	0·88	1·03	1·68	1·83	0·15 [a]
−10	3·10	3·35	4·08	4·33	0·25 [a]
20	4·05	4·50	4·60	5·05	0·45 [b]

[a] According to Ghormley and Stewart (ref. 3). [b] Schwarz, Losee, and Allen, *J. Amer. Chem. Soc.*, 1954, **76**, 4693.

This assumes further that for this purpose one can treat ice in the same way as water, ignoring the changes in crystalline structure and composition due to changes in temperature and solute concentration.

The yield of acetaldehyde obtained on irradiation of deaerated ethanol solutions decreases with decrease in temperature from 0° to −196° (Fig. 4). It is, however, almost independent of solute concentration in the range 10^{-3}—10^{-1}M-ethanol. This contrasts with the results obtained on the yield of acetaldehyde in the irradiation of oxygenated aqueous solutions of ethanol with *X*-rays at room temperature.[5]

At any one concentration of ethanol the yield of " molecular " H_2O_2 decreases with decrease in temperature below 0° (Fig. 3). Fig. 5 shows the " sudden " decrease in the yield of " molecular " hydrogen peroxide at about 0° in the irradiation of deaerated solutions of 10^{-1}—1·0M-ethanol. In addition, it indicates the almost linear decrease in the yield of hydrogen peroxide between −10° and −196°. The above data suggest that (i) the formation of " molecular " hydrogen peroxide dependent upon the diffusion and/or mobility of some reactive intermediates and (ii) the chemical reaction between these reactive species may require some activation energy. However, in the liquid phase, the yields of acetaldehyde and of hydrogen peroxide obtained on irradiation of nitrogen-saturated solutions of ethanol at 90° were the same as those obtained at 20° and at 2°.[7]

Above 10^{-1}M-ethanol the yield of acetaldehyde increases sharply with increase in the solute concentration. This increase takes place in liquid solutions irradiated at room temperature, as well as in the frozen solutions down to −196°. Table 2 gives data on the concentration-dependence of the initial yields of acetaldehyde formed on irradiation of

[7] Nixon and Weiss, unpublished results.

deaerated ethanol solutions at different temperatures. No correction has been made for the absorption of radiation by the solute at the higher ethanol concentration. The relative increase in the yields of acetaldehyde with increasing solute concentration in 1—15M-ethanol is greater for the frozen solutions at or below −78° than at room temperature (see Table 2, where yields for pure alcohol are also given).

TABLE 2. *Irradiation of aqueous ethanol with* ^{60}Co-*gamma-rays in the liquid and the frozen state. Dependence of the initial yields of acetaldehyde* (*G; molecules*/100 ev) *on the concentration of ethanol at different temperatures in the presence of* 0·1N-H_2SO_4. Dose rate 5×10^{-8} (ev/*N*) ml.$^{-1}$ min.$^{-1}$.

Ethanol (M)...		10^{-3}	10^{-2}	10^{-1}	1·0	5·0	7·5	15·0	pure
Liquid	2° and 20°	1·79	1·90	1·95	3·27	4·00	11·50	21·60	3·14
Frozen	−10°	1·10	1·20	1·45	2·16	2·75	—	—	—
	−78°	0·26	0·25	0·26	1·43	1·60	—	9·50	—
	−196°	0·27	0·27	0·27	0·40	1·05	—	6·00	3·60

The yields of acetaldehyde formed in the irradiation of ethanol solutions above 10^{1}M at room temperature, cannot be explained on the basis of the number of free radicals known to be formed is the ^{60}Co-gamma-ray radiolysis of acidified aqueous solutions, *viz.*, $G_H = 3{\cdot}7$; $G_{OH} = 2{\cdot}84$. Table 1 shows that in 1·0M-ethanol $G(-H_2O) = 5{\cdot}05$, compared with $G(-H_2O) = 4{\cdot}5$ in 10^{-3}M-ethanol.

The observed increase in the yields of the products with increasing solute concentration could be explained if one assumes (i) a further increase in the number of reactive species that become available at the higher solute concentrations, *e.g.*, by an inhibition of the back reaction $H + OH \longrightarrow H_2O$, or (ii) that propagation reactions of a chain type are initiated by unstable reactive organic intermediates formed on irradiation. Thus in the irradiation of solutions above 5·0M-ethanol at room temperature (Table 2) the yields of acetaldehyde can no longer be explained on the basis of assumption (i) and one must assume a chain reaction to take place. It was also found that the yields of oxidation product at higher solute concentrations were inversely proportional to the dose rate of the radiation. However, the suggested propagation reactions initiated by the radiation-induced species at high ethanol concentrations occur in aqueous systems only, since the yields of the oxidation products formed in the gamma-ray irradiation of pure air-free ethanol are much smaller (Table 2).

A similar effect was observed on *X*-irradiation of 2-chloroethanol;[8] the yields of hydrogen produced on irradiation of deaerated aqueous solutions at pH 1·2 increased in solute concentration over the whole range from 10^{-3}M to 3·0M-chloroethanol. Above 1·0M, in particular, the yield of hydrogen increased sharply to $G(H_2) = 6{\cdot}2$ at a solute concentration of 3·0M, but the yields of product obtained on irradiation of pure deaerated 2-chloroethanol were considerably less.

The relative increase in the yields of acetaldehyde at above 1M-ethanol is greater at −196° than at −78° or room temperature. Up to 5·0M-ethanol the increase in the products could be accounted for on the basis of a decrease in the back reaction. However, above 5·0M-ethanol the yields are so great that they cannot be a result of simple radical-solute reactions.

EXPERIMENTAL

Technique.—Solutions were irradiated with gamma-rays from a 500-Curie ^{60}Co source. The apparatus was similar to that described by Ghormley and Hochanadel.[9] About 40 ml. of solution in a cylindrical Pyrex vessel was placed inside a wide-neck Dewar flask, and fixed into position in the Co-source.

Doses were measured by means of the ferrous sulphate dosimeter, with a *G*-value of 15·5 (molecules of Fe^{3+} oxidised by 100 ev). The dose rate, measured in 0·1N-sulphuric acid solutions, was 5×10^{-8} ev/*N* ml.$^{-1}$ min.$^{-1}$.

[8] Hayon and Weiss, unpublished results.
[9] Ghormley and Hochanadel, *Rev. Sci. Instr.*, 1951, **22**, 473.

Solutions were prepared in triply-distilled water, *i.e.*, ordinary distilled water redistilled from alkaline permanganate and then from sulphuric acid. " AnalaR " ethanol was used. The irradiation vessels were cleaned with " Teepol," rinsed several times, and then washed with nitric–sulphuric acid cleaning mixture. The vessels were subsequently rinsed several times with distilled water followed by triply-distilled water.

Evacuation down to 10^{-3} mm. was by a mercury diffusion pump backed by a two-stage oil-pump.

The temperatures of 2°, −10°, −78°, and −196° were obtained by using ice, ammonium nitrate freezing mixture, Drikold–methanol freezing mixture, and liquid nitrogen respectively. After irradiation the frozen solutions were brought to room temperature by immersing the vessels in a bath through which passed a continuous flow of tap water.

Determination of Acetaldehyde.—This was based on Friedman and Haugen's method as modified by Johnson and Scholes [10] using 2,4-dinitrophenylhydrazine.

Determination of Hydrogen Peroxide.—Eisenburg's method,[11] using the titanium sulphate reagent, was here not sensitive enough to measure the small yields of hydrogen peroxide formed on irradiation. Instead, that of Egerton *et al.*[12] was used which is based on the oxidation of ferrous thiocyanate which was about ten times more sensitive. The red ferric thiocyanate formed was measured colorimetrically at 450 mμ on a " Unicam " spectrophotometer (SP.500). Calibration was carried out simultaneously by use of a hydrogen peroxide solution standardised with titanium sulphate reagent. At ethanol concentrations above 10^{-1}M, the thiocyanate method gave high values and a correction was applied.

Gas Analysis.—The gas formed on irradiation was pumped from the vessel, by means of a Töpler pump, through a trap containing liquid oxygen. The volume of gas was measured on a semimicro-burette, and collected for analysis by mass spectrometry.

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NEWCASTLE UPON TYNE. [*Received, June 9th*, 1959.]

[10] Johnson and Scholes, *Analyst*, 1954, **79**, 217.
[11] Eisenberg, *Ind. Eng. Chem. Anal.*, 1943, **15**, 327.
[12] Egerton, Everett, Minkoff, Rudrakanchana, and Salooja, *Analyt. Chim. Acta*, 1954, **10**, 422.

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788. *Steroidal αβ-Epoxy-ketones. Part I. Rearrangement of 4α,5-Epoxy-5α-cholestan-3-one and its 4β,5β-Isomer by means of the Boron Trifluoride–Ether Complex.*

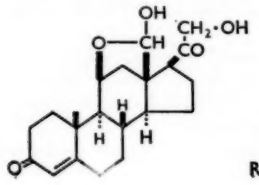
By D. J. COLLINS.

The preparation of 4α,5-epoxy-5α-cholestan-3-one is described. Treatment of 4α,5-epoxy-5α-, and 4β,5-epoxy-5β-cholestan-3-one with the boron trifluoride–ether complex in benzene solution gave, in each case, a mixture of 4-hydroxy-cholest-4-en-3-one, and A-nor-5β-cholestan-3-one. The latter is formed by spontaneous deformylation of 5-formyl-A-nor-5ξ-cholestan-3-one (XXXI), whose synthesis it had been hoped to achieve.

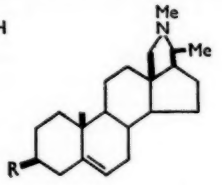
THE usual approach [1] to the partial synthesis of aldosterone (I) from steroids lacking an 18-oxygen function involves opening ring D, introducing a potential aldehyde function at position 18, and re-forming ring D. Recently, two independent groups of workers [2] reported the direct introduction, into the *intact* tetracyclic steroid molecule, of a nitrogen

[1] Heusser, Wohlfahrt, Müller, and Anliker, *Helv. Chim. Acta*, 1955, **38**, 1399; Anliker, Müller, Wohlfahrt, and Heusser, *ibid.*, p. 1404; Barton, Campos-Neves, and Scott, *J.*, 1957, 2698.
[2] Corey and Hertler, *J. Amer. Chem. Soc.*, 1958, **80**, 2903; Buchschacher, Kalvoda, Arigoni, and Jeger, *ibid.*, p. 2905.

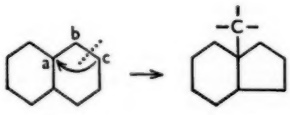
function on to $C_{(18)}$, to give steroids of the type (II). Subsequently, the Swiss group [3] announced the conversion of conessine (II; R = NMe_2) into 18-hydroxyprogesterone. The various total syntheses of aldosterone [4] involve closure of ring D in a tricyclic intermediate containing a potential 18-aldehyde function.



(I)



(II)



(III) (IV)

It would be useful if an angular aldehyde group could be created by the formal rearrangement (III) ⟶ (IV), which involves fission of bond b–c and concomitant ring closure of c to a.

In a detailed study of the acid-catalysed rearrangement of αβ-epoxy-ketones, House and Wasson [5] showed that treatment of the epoxy-ketone (V) with the boron trifluoride–ether complex in benzene, gave a mixture of the keto-aldehyde (VI) (33%), the ketone (VII) (28%), and the α-diketone (VIII) (3%). In principle, a similar rearrangement of the perhydrochrysene derivative (IX) should afford the keto-aldehyde (X), and the α-diketone (XI). Actually, the ratio of the products (X) and (XI) may be controlled by steric and stereoelectronic factors different from those operating in the case of the cyclohexane derivative (V). The more accessible compound (XII; R = C_8H_{17}), and its hitherto unknown isomer (XIII; R = C_8H_{17}), were chosen for the study of the rearrangement of αβ-epoxy-ketones in which the β-carbon is at a ring junction.

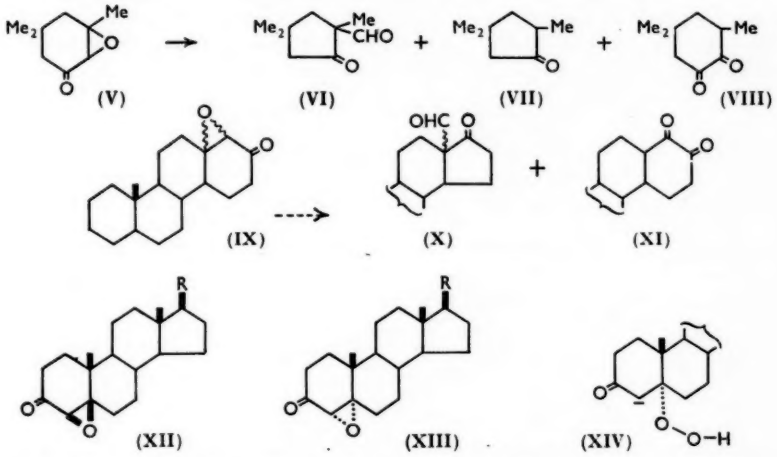
4β,5-Epoxy-5β-cholestan-3-one (XII; R = C_8H_{17}) was prepared by the action of alkaline hydrogen peroxide on cholest-4-en-3-one.[6] None of the 4α,5α-epoxide (XIII; R = C_8H_{17}), an expected by-product (cf. refs. 7—10), could be isolated from the mother-liquors of the isomer (XII; R = C_8H_{17}). If α-approach of the hydroperoxide ion to give the carbanion intermediate (XIV) (cf. ref. 11) is favoured, the predominant formation of the 4β,5β-epoxide must be due to subsequent inversion at position 5; the lack of stereospecificity of this reaction cannot be fully explained.[12]

The 4α,5α-epoxy-ketone (XIII; R = C_8H_{17}) was prepared as follows. The mixture of epimeric alcohols (XVI; R = H) and (XVII), obtained by reduction of cholest-4-en-3-one (XV) with lithium aluminium hydride,[13] was acetylated and chromatographed on alumina to give 3β-acetoxycholest-4-ene (XVI; R = Ac). Epoxidation of the latter with perbenzoic acid gave 3β-acetoxy-4α,5-epoxy-5α-cholestane (XVIII; R = Ac).[14]

When the Δ^4-acetate (XVI; R = Ac) was treated with perbenzoic acid solution which

[3] Buzzetti, Wicki, Kalvoda, and Jeger, *Helv. Chim. Acta*, 1959, **42**, 388.
[4] Lardon, Schindler, and Reichstein, *ibid.*, 1957, **40**, 666; Heusler, Ueberwasser, Wieland, and Wettstein, *ibid.*, p. 787; Schmidlin, Anner, Billeter, Heusler, Ueberwasser, Wieland, and Wettstein, *ibid.*, pp. 1034, 1438, 2291; Wieland, Heusler, Ueberwasser, and Wettstein, *ibid.*, 1958, **41**, 74, 416; Heusler, Wieland, and Wettstein, *ibid.*, p. 997; Johnson, Collins, Pappo, and Rubin, *J. Amer. Chem. Soc.*, 1958, **80**, 2585.
[5] House and Wasson, *J. Amer. Chem. Soc.*, 1957, **79**, 1488.
[6] Plattner, Heusser, and Kulkarni, *Helv. Chim. Acta*, 1948, **31**, 1822.
[7] Camerino, Patelli, and Vercellone, *J. Amer. Chem. Soc.*, 1956, **78**, 3540.
[8] Bible, Placek, and Muir, *J. Org. Chem.*, 1957, **22**, 607.
[9] Ringold, Batres, Mancera, and Rosenkranz, *ibid.*, 1956, **21**, 1432.
[10] Camerino and Patelli, *Il Farmaco* (*Pavia*) *Ed. Sci.*, 1956, **11**, 579; *Chem. Abs.*, 1957, **51**, 2007.
[11] Bunton and Minkoff, *J.*, 1949, 665.
[12] House and Ro, *J. Amer. Chem. Soc.*, 1958, **80**, 2428.
[13] (*a*) McKennis and Gaffney, *J. Biol. Chem.*, 1948, **175**, 217; (*b*) Plattner, Heusser, and Kulkarni, *Helv. Chim. Acta*, 1949, **32**, 265.
[14] Henbest and Wilson, *J.*, 1957, 1958.

contained a trace of sulphuric acid, the sole product was 3β-acetoxy-5α-cholestan-4β,5-diol (XIX; R = Ac). The latter has been tentatively assigned the 4β,5α-configuration since it was also obtained by mild acid hydrolysis of the epoxide (XVIII; R = Ac), and diaxial fission of 4α,5α-epoxides usually gives the α-configuration at position 5.[7]



Hydrolysis of the epoxy-acetate (XVIII; R = Ac) with 2% methanolic potassium hydroxide to 4α,5-epoxy-5α-cholestan-3β-ol (XVIII; R = H), followed by oxidation with chromic anhydride in pyridine, or with chromic acid in acetone, gave 4α,5-epoxy-5α-cholestan-3-one (XIII; R = C_8H_{17}), m. p. 124—125°, $[\alpha]_D$ −44°. The molecular-rotation difference of the latter and cholest-4-en-3-one (ΔM_D = −532°) is consistent with the corresponding values for other 4α,5α-epoxy-3-keto-steroids (see Table).

Molecular-rotation differences of 4α,5α-epoxy-3-keto-steroids and the parent Δ⁴-3-keto-steroids.

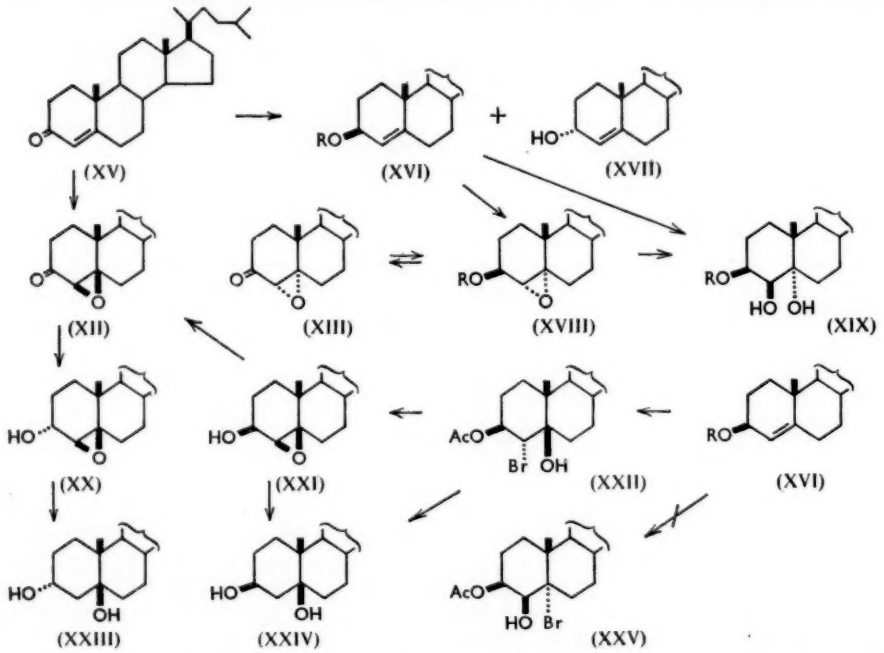
Steroid	M_D	ΔM_D	Ref.
4α,5-Epoxy-5α-cholestan-3-one	−175°	−532°	
Cholest-4-en-3-one	+357		15
4α,5-Epoxy-17β-hydroxy-17α-methyl-5α-androstan-3-one	−278	−509	9
17α-Methyltestosterone	+231		9
4α,5-Epoxy-17α,21-dihydroxy-5α-pregnane-3,11,20-trione 20-(ethylene ketal)	−46	−669	9
Cortisone 20-(ethylene ketal)	+623		16
4α,5-Epoxy-5α-androstan-3-one	−100	−440	7
Testosterone	+340		17
4α,5-Epoxy-5α-pregnane-3,20-dione	+48	−583	8
Progesterone	+631		17

The infrared spectrum of the epoxy-ketone (XIII; R = C_8H_{17}) showed bands at 889 and 861 cm.$^{-1}$, which are characteristic of steroidal αβ-epoxy-ketones.[18] The isomeric epoxy-ketone (XII) showed corresponding bands at 876 and 860 cm.$^{-1}$. Reduction of 4α,5-epoxy-5α-cholestan-3-one (XIII) with sodium borohydride regenerated 4α,5-epoxy-5α-cholestan-3β-ol (XVIII; R = H). Similar reduction of the isomeric 4β,5β-epoxy-ketone (XII) again gave an equatorial alcohol, namely, 4β,5-epoxy-5β-cholestan-3α-ol (XX).

A possible route to the 4α,5α-epoxide (XIII) from 3β-acetoxycholest-4-ene (XVI;

[15] Barton and Jones, *J.*, 1943, 602.
[16] Antonucci, Bernstein, Heller, Lenhard, Littell, and Williams, *J. Org. Chem.*, 1953, **18**, 70.
[17] Barton and Cox, *J.*, 1948, 783.
[18] Sallmann and Tamm, *Helv. Chim. Acta*, 1956, **39**, 1340; cf. Günthard, Heusser, and Fürst, *ibid.*, 1953, **36**, 1900; Patterson, *Analyt. Chem.*, 1954, **26**, 823.

R = Ac) *via* a diaxial bromohydrin with a 4α- or 5α-hydroxyl group was investigated. Addition of the elements of hypobromous acid to Δ^{2}-,[19] Δ^{11}-,[20] Δ^{16}-,[21] and $\Delta^{9(11)}$-steroids [22,23] has been accomplished by using *N*-bromosuccinimide or *N*-bromoacetamide in perchloric

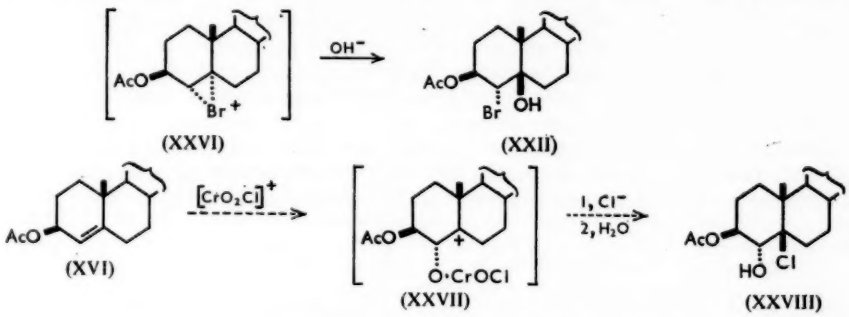


acid.[22] The reaction of Δ^{4}-steroids with this reagent does not appear to have been recorded. 3β-Acetoxycholest-4-ene (XVI; R = Ac) with *N*-bromosuccinimide in perchloric acid gave the undesired 4α-bromo-5β-acetoxy-compound (XXII), whose structure was established as follows. With methanolic potassium hydroxide it gave 4β,5-epoxy-5β-cholestan-3β-ol (XXI), m. p. 95—96°, (lit.,[6] m. p. 95—96°), which with chromic acid in acetone gave 4β,5-epoxy-5β-cholestan-3-one (XII). The bromohydrin must therefore have a β-oriented hydroxyl group, and must be (XXII) rather than (XXV) since it was unaffected by chromic acid in acetone. Reduction of the bromohydrin with lithium aluminium hydride gave, albeit in poor yield, the 3β,5β-diol (XXIV), which was similarly obtained from the epoxy-alcohol (XXI).[24] This does not permit distinction between structures (XXII) and (XXV), since reduction of the bromohydrin may proceed *via* the epoxide (XXI) (cf. the reduction of certain α-bromo-ketones [25]) which could be obtained from either (XXII) or (XXV). Supporting evidence for structure (XXII) for the bromohydrin is the fact that the frequency of the 3β-acetate carbonyl absorption band (1748 cm.$^{-1}$) is higher than normal (*ca.* 1736 cm.$^{-1}$), a phenomenon which has been observed for 3β-acetoxy-5β-hydroxy-steroids and has been attributed to interaction of the two groups by virtue of their proximity in space.[26] The structure of the bromohydrin (XXII) can be rationalised by assuming

[19] Slates and Wendler, *J. Amer. Chem. Soc.*, 1956, **78**, 3749.
[20] Herz, Fried, and Sabo, *ibid.*, p. 2017.
[21] Löken, Kaufmann, Rosenkranz, and Sondheimer, *ibid.*, p. 1738.
[22] Fried and Sabo, *ibid.*, 1953, **75**, 2273; 1957, **79**, 1130.
[23] Herr, Hogg, and Levin, *ibid.*, 1956, **78**, 500.
[24] Plattner, Heusser, and Kulkarni, *Helv. Chim. Acta*, 1948, **31**, 1885.
[25] Henbest, Jones, Wagland, and Wrigley, *J.*, 1955, 2477.
[26] Nickon, *J. Amer. Chem. Soc.*, 1957, **79**, 243.

α-attack of bromonium ion to give the cation (XXVI), followed by β-attack of hydroxyl ion to give the bromohydrin (XXII). This mechanism requires abnormal fission of the 5α-axial bond of the 4α,5α-bromonium ion (XXVI), rather than the expected 4α-equatorial bond-fission * [cf. the hydrolysis of the 4α,5α-epoxide (XVIII; R = Ac) mentioned above].

It has been shown [19] that treatment of a Δ^2-steroid with chromyl chloride affords a chlorohydrin which is *positionally* isomeric with that which is obtained by the action of hypohalous acid. However, the reaction of the Δ^4-steroid (XVI) with chromyl chloride



failed to give the expected chlorohydrin (XXVIII), which theoretically could have been formed *via* the cation (XXVII) (cf. Cristol and Eilar [27]).

The boron trifluoride–ether complex has been used in the rearrangement of αβ-unsaturated-,[28] α-hydroxy-,[29] and simple steroidal epoxides.[30] Also, its reaction with 3-substituted 5α,6α- and 5β,6β-epoxy-steroids has been studied,[31] but no systematic examination of its effect on steroidal αβ-epoxy-ketones has been recorded. In a preliminary report on the preparation of 4-substituted testosterone analogues, Camerino *et al.*[7] stated that treatment of 4α,5-epoxy-17β-hydroxy-5α-androstan-3-one (XIII; R = OH), and its 4β,5β-isomer (XII; R = OH), with the boron trifluoride–ether complex in benzene gave 4-hydroxytesterone. The yield was not given, and no mention was made of any by-products.

When 4β,5-epoxy-5β-cholestan-3-one (XII) was treated with one equivalent of the boron trifluoride–ether complex in benzene for 5 min., a mixture of the starting epoxy-ketone and 4-hydroxycholest-4-en-3-one (XXXVI) was obtained. With a reaction period of 18½ hr. there resulted a complex mixture from which was isolated 35% of the enolic diketone (XXXVI), and 3% of 5β-A-norcholestan-3-one (XXXIII). The latter must be formed *via* the desired keto-aldehyde (XXXI) by deformylation either in the reaction mixture or during the subsequent chromatography for which neutral alumina was used. In an attempt to trap the angular aldehyde group *in situ*, the 4β,5β-epoxy-ketone (XII) was refluxed for 6 hr. with ethylene glycol and the boron trifluoride–ether complex in benzene under a water-separator. Chromatography of the gummy product gave 4% of 5β-A-norcholestan-3-one (XXXIII), and 2·6% of a substance, m. p. 176—177°,

* Grateful acknowledgment is made to one of the referees for drawing attention to this point.

[27] Cristol and Eilar, *J. Amer. Chem. Soc.*, 1950, **72**, 4353.

[28] Heusser, Eichenberger, Kurath, Dällenbach, and Jeger, *Helv. Chim. Acta*, 1951, **34**, 2106; Heusser, Heusler, Eichenberger, Honegger, and Jeger, *ibid.*, 1952, **35**, 295; Heusler and Wettstein, *ibid.*, 1953, **36**, 398; Budziarek, Johnson, and Spring, *J.*, 1952, 3410; Bladon, Henbest, Jones, Lovell, Wood, and Woods; Elks, Evans, Hathway, Oughton, and Thomas, *J.*, 1953, 2921; Elks, Evans, Robinson, Thomas, and Wyman, *ibid.*, p. 2933; Henbest and Wagland, *J.*, 1954, 728.

[29] Heusser, Anliker, Eichenberger, and Jeger, *Helv. Chim. Acta*, 1952, **35**, 936; Djerassi and Lemin, *J. Amer. Chem. Soc.*, 1954, **76**, 5672.

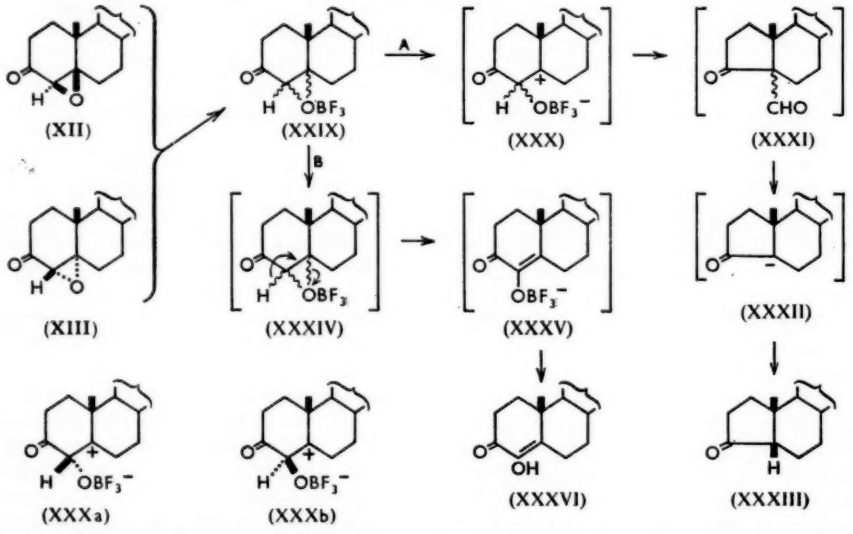
[30] Henbest and Wrigley, *J.*, 1957, 4596.

[31] *Idem, ibid.*, p. 4765.

which showed neither hydroxyl nor carbonyl absorption in the infrared spectrum and gave analyses for the bis(ethylene ketal) of (XXXI) or of the keto-form of (XXXVI). Acid-hydrolysis and deformylation of the former should have afforded the A-nor-3-ketone (XXXIII); the compound, m. p. 176—177°, was unaffected by aqueous acetic acid in dioxan at 100°. Owing to the low yield of this substance it was not studied further.

4α,5-Epoxy-5α-cholestan-3-one (XIII) was recovered unchanged after treatment with the boron trifluoride–ether complex in benzene for 15 min., but with a reaction period of 23 hr. there was obtained 5β-A-norcholestan-3-one (XXXIII) (25%), and 4-hydroxycholest-4-en-3-one (XXXVI) (30%). It has been observed that the substitution of ether for benzene as solvent greatly retards the rate of rearrangement of αβ-unsaturated epoxides by the boron trifluoride–ether complex (Bladon *et al.*[28]), and in the case of benzylideneacetophenone oxide [32] causes the formation of a fluorohydrin rather than a β-keto-aldehyde. In the present instance, the 4α,5α-epoxy-ketone (XIII) was unaffected by the boron trifluoride–ether complex in refluxing ether.

The rearrangement of the epoxy-ketones (XII) and (XIII) may be regarded as proceeding by the two paths A and B (cf. House [5,32]). The initially formed co-ordination complex (XXIX) could afford the carbonium ion (XXX), which by acyl-migration would give the



keto-aldehyde (XXXI). Deformylation of either the 5α- or the 5β-isomer of the latter, involving formation and protonation of the anion (XXXII), would give the A/B-*cis*-fused A-nor-3-ketone (XXXIII). The undescribed 5α-isomer of (XXXIII) was not isolated in any of these experiments. Alternatively, loss of a proton by the electron-shift (XXXIV), and hydrolysis of the intermediate (XXXV), would give the enolic diketone (XXXVI). The yield of the A-nor-3-ketone (XXXIII) was approximately ten times greater from the rearrangement of the 4α,5α-epoxy-ketone (XIII) than from its 4β,5β-isomer (XII). This is explicable on the basis that the intermediate carbonium ion (XXXa) is more stable than its isomer (XXXb) owing to the 1,3-diaxial interactions of the bulky, quasi-axial $-O\cdot BF_3$ group in the latter. Also, the stereochemistry at position 4 in the carbonium ion (XXX) may affect the rate of acyl-migration.

If the presumed intermediate β-keto-aldehyde (XXXI) has the 5α-configuration, it may be possible to prevent deformylation by having present in the molecule a 7α-hydroxyl

[32] House, *J. Amer. Chem. Soc.*, 1956, **78**, 2298.

group which would be favourably situated for hemiacetal formation. The main problem is to promote rearrangement by path A (β-keto-aldehyde formation) rather than by path B (α-diketone formation). It is intended to do further work in this direction.

Experimental

Infrared spectra were measured with a Perkin–Elmer model 21 double-beam spectrophotometer. Ultraviolet spectra were measured with a Unicam SP. 500 spectrophotometer for ethanol solutions. Optical rotations refer to chloroform solutions. Unless stated otherwise, B.D.H. alumina was used. Light petroleum refers to the fraction of b. p. 40—70°.

4β,5-Epoxy-5β-cholestan-3-one (XII; R = C_8H_{17}).—4β,5-Epoxy-5β-cholestan-3-one was prepared by the action of alkaline hydrogen peroxide on cholest-4-en-3-one.[6] The epoxy-ketone crystallised from chloroform–methanol as prisms, m. p. 118—119°, $[\alpha]_D$ +124°, $\nu_{max.}$ (in Nujol) 1718s (C=O), 1247m, 876m, and 860s (epoxide) (lit.,[6] m. p. 116—117°, $[\alpha]_D^{21}$ +134°, 136°).

The mother-liquors were evaporated and chromatographed on alumina. Although it is almost certainly present, the 4α,5α-epoxy-ketone (XIII; R = C_8H_{17}) could not be obtained.

Reduction of 4β,5-Epoxy-5β-cholestan-3-one with Sodium Borohydride.—A solution of 4β,5-epoxy-5β-cholestan-3-one (200 mg.) in 80% dioxan–water (14 ml.) was treated with sodium borohydride (40 mg.) in the same solvent (4 ml.). The mixture was kept for 48 hr. at room temperature, then excess of reagent was decomposed with acetic acid (2 drops), and the mixture was poured into ice-water (100 ml.). The precipitate, m. p. 135—148°, was chromatographed in 50% benzene–light petroleum on alumina. Elution with benzene (130 ml.) gave a solid (170 mg.), which after several recrystallisations from methanol gave 4β,5-epoxy-5β-cholestan-3α-ol (XX) as laths, m. p. 161—162°, $[\alpha]_D$ +25° (lit.,[6] m. p. 158—159°, $[\alpha]_D$ +31·4°).

5β-Cholestane-3α,5-diol (XXIII).—The epoxy-alcohol (XX) (150 mg.) was reduced with lithium aluminium hydride (100 mg.) in the usual way. Recrystallisation of the product from methanol gave 5β-cholestane-3α,5-diol (XXIII) as laths m. p. 190—192·5°, $[\alpha]_D$ +35° (lit.,[6] m. p. 192—193°, $[\alpha]_D$ +47·3°).

3β-Acetoxycholest-4-ene (XVI; R = Ac).—Cholest-4-en-3-one (12·0 g.) was reduced with lithium aluminium hydride (1·5 g.) in ether to a mixture of the epimeric alcohols (XVI; R = H), and (XVII).[13] The crude product was treated at room temperature overnight with acetic anhydride (25 ml.) in pyridine (120 ml.). The mixture was poured on ice-water (1·5 l.). The gummy acetates were isolated with benzene, and chromatographed in light petroleum on acid-washed alumina (170 g.). Elution with light petroleum (350 ml.) gave a solid (10·1 g.), which after crystallisation from ethanol gave 3β-acetoxycholest-4-ene (7·5 g.), m. p. 86°, $[\alpha]_D$ +10° (lit.,[13a] m. p. 85°).

Reduction of this acetate with lithium aluminium hydride gave cholest-4-en-3β-ol (XVI; R = H), m. p. 131—132°, $[\alpha]_D$ +53°, needles from ethanol (lit.,[13b] m. p. 131—132°, $[\alpha]_D^{22}$ +44·6°).

Action of Perbenzoic Acid on 3β-Acetoxycholest-4-ene.—(a) *3β-Acetoxy-4α,5-epoxy-5α-cholestane* (XVIII; R = Ac). To a cooled solution of 3β-acetoxycholest-4-ene (1·0 g.) in chloroform (50 ml.) was added a cold 0·28M-chloroform solution (10 ml.) of perbenzoic acid. The mixture was kept overnight at room temperature, washed with water, dried (Na_2SO_4), and passed through neutral alumina (30 g.; Woelm grade 1). Evaporation of the chloroform eluate (100 ml.) under reduced pressure gave a solid which on trituration with methanol gave crystals, m. p. 100—112°. Two recrystallisations from methanol afforded 3β-acetoxy-4α,5-epoxy-5α-cholestane (640 mg., 62%), m. p. 119—120° $[\alpha]_D$ +55° (lit.,[14] m. p. 117—119°, $[\alpha]_D$ +60°).

(b) *3β-Acetoxy-5α-cholestane-4β,5-diol* (XIX; R = Ac). To a solution of 3β-acetoxycholest-4-ene (1·0 g.) in chloroform (50 ml.) at 0° was added a 0·51M-chloroform solution (7 ml.) of perbenzoic acid containing a trace of sulphuric acid. After being kept overnight at room temperature, the chloroform solution was washed with 10% sodium carbonate solution and water, dried (Na_2SO_4), and evaporated. Several recrystallisations of the residue from acetone–methanol gave *3β-acetoxy-5α-cholestane-4β,5-diol* (500 mg.) as matted needles m. p. 199°, $[\alpha]_D$ +23°, $\nu_{max.}$ (in Nujol) 3528, 3589 (OH), 1712 $cm.^{-1}$ (OAc) (Found: C, 75·4; H, 10·9. $C_{29}H_{50}O_4$ requires C, 75·3; H, 10·9%).

Mild Acid-hydrolysis of 3β-Acetoxy-4α,5-epoxy-5α-cholestane.—A solution of the epoxy-acetate (100 mg.) in acetone (25 ml.) and water (2·5 ml.) containing 2N-sulphuric acid (0·2 ml.) was kept at room temperature for 48 hr. After removal of the acetone under reduced pressure, water was added, and the product was isolated with ether. Three recrystallisations from

acetone–methanol gave needles, m. p. 198—199° alone or mixed with 3β-acetoxy-5α-cholestane-4β,5-diol obtained as described above.

5α-Cholestane-3β,4β,5-triol (XIX; R = H).—(*a*) Hydrolysis of 3β-acetoxy-5α-cholestane-4β,5-diol (100 mg.) for 2 hr. with refluxing 2% methanolic potassium hydroxide (12 ml.) afforded the *triol monohydrate*, m. p. 215—216°, $[\alpha]_D$ +43° in pyridine, needles (from aqueous methanol) (Found: C, 74·1; H, 11·6. $C_{27}H_{48}O_3,H_2O$ requires C, 73·9; H, 11·5%).

The same triol was obtained by reduction of the monoacetate (XIX; R = Ac) with lithium aluminium hydride.

4α,5-Epoxy-5α-cholestan-3-one (XIII; R = C_8H_{17}).—3β-Acetoxy-4α,5-epoxy-5α-cholestane (XVIII; R = Ac) (100 mg.) was refluxed with 2% methanolic potassium hydroxide (12 ml.) for 1 hr. Removal of most of the methanol *in vacuo* and addition of water gave a solid, m. p. 135—136°. Recrystallisation of this from aqueous ethanol gave 4α,5-epoxy-5α-cholestan-3β-ol (XVIII; R = H) as needles m. p. 136—137°, $[\alpha]_D$ +54°.

To a stirred solution of this epoxy-alcohol (1·0 g.) in acetone (100 ml.) was added dropwise 1·45 ml. of chromic acid solution which was prepared by dissolving chromic anhydride (6·67 g.) in water (10 ml.) and concentrated sulphuric acid (5·33 ml.) and diluting it to 25 ml. with water.[33] After addition of a few drops of methanol, the product was isolated in the usual manner and adsorbed on alumina (40 g.) from light petroleum. Elution with 8 : 92 benzene–light petroleum gave a solid which on crystallisation from methanol afforded *4α,5-epoxy-5α-cholestan-3-one* (610 mg.) as blades, m. p. 123—124·5°, $[\alpha]_D$ −44°, $\nu_{max.}$ (in Nujol) 1714s (C=O), 1244m, 889m, 861m cm.$^{-1}$ (epoxide) (Found: C, 81·3; H, 11·0. $C_{27}H_{44}O_2$ requires C, 80·94; H, 11·1%).

Oxidation of the epoxy-alcohol (XVIII; R = H) with chromic anhydride in pyridine gave a slightly better yield of the epoxy-ketone (XIII), but the formation of a stable emulsion during isolation of the product made this method inconvenient.

Reduction of 4α,5-Epoxy-5α-cholestan-3-one (XIII; R = C_8H_{17}) *with Sodium Borohydride.*—To a solution of the epoxy-ketone (100 mg.) in 4 : 1 dioxan–water (8 ml.) was added a solution of sodium borohydride (20 mg.) in the same solvent (2 ml.). After the mixture had been kept at room temperature for 45 hr., excess of reagent was decomposed with acetic acid (2 drops), and the mixture poured into ice-water (20 ml.). The crude product, m. p. 120°, was adsorbed on alumina (5 g.) from 1 : 4 benzene–light petroleum. Elution with 1 : 99 ether–benzene gave a solid (75 mg.) which on crystallisation from aqueous methanol gave 4α,5-epoxy-5α-cholestan-3β-ol (XVIII; R = H), m. p. 136—137°, undepressed on admixture with the epoxy-alcohol obtained by hydrolysis of 3β-acetoxy-4α,5-epoxy-5α-cholestane (XVIII; R = Ac).

4α-Bromo-5β-cholestane-3β,5-diol 3-Acetate (XXII).—To a solution of 3β-acetoxycholest-4-ene (900 mg.) in dioxan (30 ml.) was added powdered *N*-bromosuccinimide (4·8 g.). The suspension was cooled in an ice-bath, and 10% aqueous perchloric acid (22·5 ml.) added dropwise with stirring. The mixture was stirred for a further 3 hr., then 5% sodium hydrogen sulphite solution (10 ml.) and water (60 ml.) were added. The white precipitate melted at 140°. Several recrystallisations from light petroleum gave *4α-bromo-5β-cholestane-3β,5-diol 3-acetate*, as plates, m. p. 147° (decomp.), $[\alpha]_D$ +32°, $\nu_{max.}$ (in CS_2) 3650 (OH), 1748 cm.$^{-1}$ (acetate C=O) (Found: C, 66·2; H, 9·4; Br, 15·7. $C_{29}H_{49}O_3Br$ requires C, 66·3; H, 9·4; Br, 15·2%).

4β,5-Epoxy-5β-cholestan-3β-ol (XXI).—To a suspension of the above bromohydrin (120 mg.) in methanol (10 ml.) was added a solution of potassium hydroxide (100 mg.) in water (0·15 ml.) and methanol (1·0 ml.). The solid rapidly dissolved. The solution was refluxed for 30 min., then concentrated *in vacuo* and diluted with water (10 ml.). Recrystallisation of the precipitate from aqueous methanol gave 4β,5-epoxy-5β-cholestan-3β-ol as needles, m. p. 96—97° (lit.,[13b] m. p. 95—96°).

Oxidation of this epoxy-alcohol (17 mg.) in acetone (2 ml.) with 0·3 ml. of chromic acid solution (prepared as described above), and two recrystallisations of the product from chloroform–methanol afforded 4β,5-epoxy-5β-cholestan-3-one, m. p. and mixed m. p. 118—119°.

Attempted Oxidation of the Bromohydrin (XXII) *with Chromic Acid.*—To a solution of the bromohydrin (100 mg.) in acetone (10 ml.) was added chromic acid solution (0·15 ml.; prepared as before), dropwise with shaking. The product crystallised from methanol as plates, m. p. and mixed m. p. with the starting material, 147°. The hydroxyl group of the bromohydrin must therefore be tertiary.

Reduction of the Bromohydrin (XXII) *with Lithium Aluminium Hydride.*—A solution of the bromohydrin (100 mg.) in ether (20 ml.) was added dropwise to a slurry of lithium aluminium

[33] Bladon, Fabian, Henbest, Koch, and Wood, *J.*, 1951, 2402.

hydride (60 mg.) in ether (30 ml.), and the mixture was refluxed 30 min. The product was adsorbed on alumina (3·0 g.) from 1 : 1 benzene–light petroleum. Elution with 4 : 96 ether–benzene (60 ml.) gave 5β-cholestane-3β,5-diol (25 mg.) which crystallised from aqueous methanol as needles, m. p. 143—144°, undepressed on admixture with a specimen prepared as below.

Elution with 1 : 4 ether–benzene (100 ml.) gave a solid (50 mg.), m. p. 178—188°, which gave a negative Beilstein test for halogen. Two recrystallisations from aqueous methanol gave needles of a substance, m. p. 185—190°, which was depressed on admixture with 5β-cholestane-3α,5-diol, m. p. 190—192·5°. Since the physical constants of the other epimeric 3,5-diols are different, the product of m. p. 185—190° is probably a dimer formed by bimolecular reduction.

5β-Cholestane-3β,5-diol (XXIV).—Reduction of 4β,5-epoxy-5β-cholestan-3β-ol (XXI) with lithium aluminium hydride, and crystallisation of the product from light petroleum gave the 3β,5β-diol as prisms, m. p. 147—149°, $[\alpha]_D$ +40° (lit.,[24] m. p. 148—149°, $[\alpha]_D$ +52·3°).

Action of Chromyl Chloride on 3β-Acetoxycholest-4-ene.—Treatment of 3β-acetoxycholest-4-ene with chromyl chloride (cf. Slates and Wendler [19]) gave a green halogen-containing gum which with methanolic potassium hydroxide or with chromic acid in acetone, followed in each case by chromatography on alumina, failed to give a crystalline epoxide or ketone respectively.

Action of the Boron Trifluoride–Ether Complex on 4β,5-Epoxy-5β-cholestan-3-one (XII; R = C_8H_{17}).—(*a*) To a solution of the epoxy-ketone (1·0 g.) in dry benzene (20 ml.) was added freshly distilled boron trifluoride–ether complex (0·31 ml.). The mixture, which became greenish-yellow, was kept at room temperature for 5 min., diluted with ether (25 ml.), and washed with 10% aqueous sodium hydrogen carbonate, then with water, dried (Na_2SO_4), and evaporated. The gummy residue was dissolved in light petroleum and adsorbed on neutral alumina (30 g.; Woelm grade 1). Elution with 8 : 92 benzene–light petroleum and with benzene gave a total of 330 mg. of a solid, crystallisation of which from methanol gave 4β,5-epoxy-5β-cholestan-3-one, m. p. and mixed m. p. 117—119°. Elution with ether, and recrystallisation of the solid thus obtained, gave 4-hydroxycholest-4-en-3-one (250 mg.) as needles, m. p. 147—148°, $[\alpha]_D$ +84°, $\lambda_{max.}$ 279 mμ (13,260 in EtOH), $\nu_{max.}$ (in Nujol) 3420 (ON), 1665, 1632 cm.$^{-1}$ (enolic α-diketone) {Lit.,[34] m. p. 151°, $[\alpha]_D$ +80°, $\lambda_{max.}$ 278 mμ (13,000 in EtOH)}.

(*b*) The reactants (same quantities) were mixed and kept at room temperature for 18½ hr. The product was isolated as before and chromatographed on neutral alumina (30 g.; Woelm grade 1). Elution with 1 : 99 ether–benzene (100 ml.) gave a solid (35 mg., 4%), which after two recrystallisations from methanol gave 5β-A-norcholestan-3-one (XXXIII) as prisms, m. p. 76·5°, $[\alpha]_D$ +130°, $\nu_{max.}$ (in Nujol) 1740 cm.$^{-1}$ (5-ring ketone) (lit.,[35] m. p. 73·5—74·5°, $[\alpha]_D$ +105° (measured before purification), $\nu_{max.}$ (in CS_2) 1736 cm.$^{-1}$}. Elution with ether gave 4-hydroxycholest-4-en-3-one (350 mg.), m. p. 144—146°.

Action of the Boron Trifluoride–Ether Complex and Ethylene Glycol on 4β,5-Epoxy-5β-cholestan-3-one (XII; R = C_8H_{17}).—A mixture of the epoxy-ketone (1·0 g.), ethylene glycol (2 ml.), and the boron trifluoride–ether complex (0·3 ml.) in benzene (50 ml.) was refluxed for 6 hr. under a water-separator. The cooled mixture was washed with water, dried (Na_2SO_4), and evaporated. The residue was adsorbed on neutral alumina (30 g.; Woelm grade 1). Elution with 3 : 1 benzene–light petroleum (100 ml.) gave 31 mg. (2·6%) of crystals, m. p. 175°, which after two recrystallisations from chloroform–methanol afforded needles of a *bis-dioxolan*, m. p. 176—177° (the infrared spectrum showed neither hydroxyl nor carbonyl absorption) (Found: C, 76·4; H, 10·7. $C_{31}H_{52}O_4$ requires C, 76·2; H, 10·7%). This compound resisted hydrolysis with aqueous acetic acid in dioxan at 100°.

Elution with 1 : 99 ether–benzene gave 5β-A-norcholestan-3-one (40 mg.), m. p. and mixed m. p. 76°. No other crystalline products were obtained.

Action of the Boron Trifluoride–Ether Complex on 4α,5-Epoxy-5α-cholestan-3-one (XIII; R = C_8H_{17}).—(*a*) A solution of the epoxy-ketone (250 mg.) in benzene (6 ml.) was treated with freshly distilled boron trifluoride–ether complex (0·08 ml.). The mixture rapidly became yellow, then pale orange. After 23 hr. the mixture was diluted with ether (30 ml.), washed with 10% aqueous sodium hydrogen carbonate, then with water, dried (Na_2SO_4), and evaporated *in vacuo*. The pale lemon oily residue was chromatographed in light petroleum on neutral

[34] Fieser and Stevenson, *J. Amer. Chem. Soc.*, 1954, **76**, 1728.
[35] Smith and Nace, *J. Amer. Chem. Soc.*, 1954, **76**, 6119.

alumina (10 g.; Woelm grade I). Elution with 1 : 1 benzene–light petroleum gave 5β-A-norcholestan-3-one (64 mg., 25%), m. p. and mixed m. p. 74—75°. Elution with ether gave 4-hydroxycholest-4-en-3-one, m. p. 146—148° (30%).

When the same quantities of reactants were used and the reaction period was 15 min., the only crystalline material isolated was the starting epoxy-ketone (120 mg.).

(*b*) A solution of the epoxy-ketone (250 mg.) in dry ether (15 ml.) was treated with the boron trifluoride–ether complex (0·08 ml.) and left at room temperature for 22 hr., then diluted with ether (40 ml.) and worked up as before. The product crystallised from methanol as needles, m. p. 124—125°, undepressed on admixture with the starting material.

When a solution of the epoxy-ketone (250 mg.) and the boron trifluoride–ether complex (0·08 ml.) in dry ether (15 ml.) was refluxed for 4 hr., the product from the washed, dried (Na_2SO_4) ether extract, melted at 120—123° and did not depress the m. p. of the starting material.

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789. *New Intermediates and Dyes. Part VII.* The Influence of the t-Butyl Group on the Properties of Azoic Dyes.*

By (MRS.) V. VASSILIADIS and ARNOLD T. PETERS.

o-, *m*-, and *p*-t-Butylaniline have been used as diazotisable amines and also to prepare coupling components, for a series of azo-dyes; the latter were prepared in substance and also tested as azoic dyes on cotton.

In general, the presence of the t-butyl group produced a slight hypsochromic effect, and somewhat less colour strength, when compared with analogous dyes containing the methyl group.

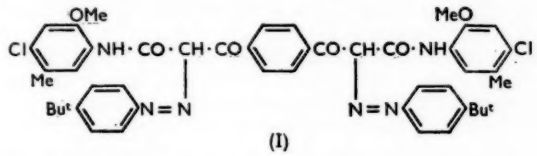
t-BUTYLBENZENE, best prepared by the method of Bromby, Peters, and Rowe,[1] gave 86% of *p*-nitro-t-butylbenzene,[2] thence reduced in 71% yield to *p*-t-butylaniline by a modification of the method [3] employed for preparing 2,3,5,6-tetrachloroaniline.

p-t-Butylaniline was condensed with 3-hydroxy-2-naphthoic acid in boiling toluene in presence of phosphorus trichloride, giving 89% of 3-hydroxy-*N*-*p*-t-butylphenyl-2-naphthamide, which has been used as coupling component for azoic dyes; the analogous *N*-*p*-tolyl compound was prepared for comparison. *p*-t-Butylaniline was readily diazotised at 5°, and formed a stabilised diazo-compound, isolated as the zinc chloride double salt or after condensation with sarcosine. For diazotisation and preparation of dyes, the crystalline hydrochloride of the base was used, as otherwise some insoluble resin was formed. Diazotised *p*-t-butylaniline was coupled with the *N*-phenyl (Naphtol AS), *N*-*o*-tolyl (AS-D), and *N*-4-methoxy-2-methylphenyl derivative (AS-LT) of 3-hydroxy-2-naphthamide, to give the corresponding azoic dyes; yellow dyes were obtained by coupling with terephthaloyl compound (I) (AS-L3G) and 2,2′-di(acetoacetamido)biphenyl (Brenthol AT), and a brown shade was derived from 3-(*N*-*p*-chlorophenylcarbamoyl)-2-hydroxycarbazole (Brenthol BT). By using our butylanilide as coupling component, the bright red dye (II) was obtained in 88% yield.

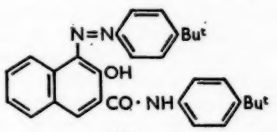
* Part VI, *J.*, 1958, 3497.

[1] Bromby, Peters, and Rowe, *J.*, 1943, 144.
[2] Craig, *J. Amer. Chem. Soc.*, 1935, **57**, 195.
[3] Peters, Rowe, and Stead, *J.*, 1943, 233.

Azoic dyes were also prepared in quantity from diazotised 1-naphthylamine (brownish-violet dye), 2,5-dichloroaniline (bright red), 2-nitro-*p*-toluidine (red), and 4-nitroaniline (deep red), by coupling with the new anilide. In general, azoic dyeings on cotton of the above dyes containing the *p*-t-butyl group showed bright shades of good colour strength,



(I)



(II)

very similar to those derived from the corresponding *p*-methyl analogues, but with a slight hypsochromic effect.

o-t-Butylaniline [4] was converted in 61% yield into 3-hydroxy-*N*-*o*-t-butylphenylnaphthamide (A). The diazonium chloride solution obtained from *o*-t-butylaniline or its hydrochloride decomposed quickly, and quick coupling was effected at below 0°, to yield red, yellow, and brown azo-dyes, as above. Such dyes gave weaker shades on cotton than those derived from analogous dyes obtained from the more readily handled *o*-toluidine and the same coupling components. 3-Hydroxy-*N*-*o*-t-butylphenyl-4-*o*-t-butylphenylazo-2-naphthamide, a bright red dye (75% yield), gave a pink shade on cotton, but it possessed less colour strength than the di-*p*-t-butyl analogue. The use of the anilide (A) as coupling component with a series of diazotised amines yielded azoic dyeings of good colour strength, only slightly weaker than the dyeings of similar shade obtained from the corresponding 2'-methyl analogues.

o-Nitro-t-butylbenzene was converted by zinc in boiling aqueous-methanolic sodium-hydroxide into 2,2-di-t-butylhydrazobenzene in 50% yield, and thence by aqueous hydrochloric acid in ether into 3,3'-di-t-butylbenzidine dihydrochloride (30%). The last product was tetrazotised, to give a moderately stable diazo-solution, which coupled with the *o*-toluidide and *p*-t-butylanilide of 3-hydroxy-2-naphthoic acid to give dark violet-blue bisazo-dyes. Dyeings were slightly redder in shade, but less deep than those obtained similarly from 3,3'-dimethylbenzidine.

m-t-Butylaniline [5] gave the anilide of 3-hydroxy-2-naphthoic acid in 88% yield. This amine afforded a stable diazonium salt, which coupled readily to yield a series of azoic dyes; *e.g.*, the red 3-hydroxy-*N*-*m*-t-butylphenyl-4-*m*-t-butylphenylazo-2-naphthamide was prepared in 90% yield. Azoic dyes obtained from diazotised *m*-t-butylaniline or the derived anilide gave shades and colour strength on cotton almost identical with those derived from the *m*-methyl analogues.

Experimental

p-t-Butylaniline.—A mixture of ethanol (300 ml.), hydrochloric acid (6 ml.), and iron powder (40 g.) was refluxed for 15 min. to activate the iron; to the boiling and stirred mixture, *p*-t-butylnitrobenzene [2] (27 g.), b. p. 127—132°/10 mm., m. p. 18°, was added during 1 hr. After refluxing for a further 5 hr., the mixture was made alkaline with sodium carbonate and filtered, most of the ethanol was removed from the filtrate, water added, and the mixture was extracted with benzene; the benzene extract was dried and evaporated; dilute hydrochloric acid was added and the mixture extracted with benzene to remove unchanged *p*-t-butylnitrobenzene. The dilute hydrochloric acid solution was neutralised with aqueous ammonia, and the amine extracted with benzene. *p*-t-Butylaniline was distilled as a pale yellow oil, b. p. 110—112°/12 mm. (16 g., 71·2%), and gave an acetyl derivative, plates, m. p. 169—171° (lit.,[5] m. p. 171°). The derived colourless crystalline hydrochloride, diazotised in aqueous hydrochloric acid, was converted into stabilised diazonium salts, by addition of zinc chloride and aqueous sodium chloride, or by addition to sarcosine in aqueous sodium chloride and sodium carbonate. Both salts were stable and the diazonium chloride was readily liberated by hydrochloric acid.

[4] Shoesmith and Mackie, *J.*, 1928, 2334.
[5] Carpenter, Easter, and Wood, *J. Org. Chem.*, 1951, **16**, 586.

3-Hydroxy-N-p-t-butylphenyl-2-naphthamide(B).—3-Hydroxy-2-naphthoic acid (14 g.), *p*-t-butylaniline (11 g.), and toluene (128 g.) were heated at 75—77°, and phosphorus trichloride (3 ml.) was added during 1 hr. After refluxing for a total of 4 hr., the mixture was cooled and neutralised with aqueous sodium carbonate. Toluene was removed in steam, and the residue collected, washed, and dried (21 g., 89%). The p-*t-butylanilide* crystallised from ethanol in buff-coloured prismatic needles, m. p. 249—250° (Found: C, 78·7; H, 6·7; N, 4·2. $C_{21}H_{21}O_2N$ requires C, 79·0; H, 6·6; N, 4·4%).

3-Hydroxy-N-p-tolyl-2-naphthamide.—3-Hydroxy-2-naphthoic acid (18·8 g.), *p*-toluidine (10·7 g.), toluene (120 ml.), and phosphorous trichloride (4 ml.) gave, as above, the p-*toluidide* (23·5 g., 84·8%), which crystallised from chlorobenzene in straw-coloured plates, m. p. 222° (Found: C, 77·8; H, 5·4; N, 5·2. $C_{18}H_{15}O_2N$ requires C, 78·0; H, 5·4; N, 5·0%).

Azoic Dyes from p-*t-Butylaniline.*—The hydrochloride (0·93 g.) of *p*-t-butylaniline was dissolved in hot water (6 ml.), the solution was cooled, and hydrochloric acid (1 ml.) was added with stirring; diazotisation was effected at 5° by adding sodium nitrite (0·4 g.) in water (4 ml.). The clear diazo-solution was coupled with an alkaline solution of the appropriate component in slight excess, at 5°.

Thus, Naphtol AS (1·5 g.) gave the azo-dye (1·8 g., 85·3%), which was purified by chromatography in xylene on alumina; elution with xylene, followed by crystallisation from the same solvent, gave red prisms, m. p. 195—196°, of *3-hydroxy-4-p-t-butylphenylazo-2-naphthanilide* (Found: C, 76·3; H, 5·8; N, 9·8. $C_{27}H_{25}O_2N_3$ requires C, 76·6; H, 5·9; N, 9·9%). Similarly were prepared from the appropriate Naphtol: *Red dyes:* the o-*toluidide* (82·5%), purified by benzene–alumina, and crystallised from benzene in red prismatic needles, m. p. 214—215° (Found: C, 76·4; H, 6·0; N, 9·6. $C_{28}H_{27}O_2N_3$ requires C, 76·9; H, 6·2; N, 9·6%); the 4-*methoxy*-o-*toluidide* (81·5%), deep red needles (from benzene), m. p. 191—192° (Found: C, 74·3; H, 6·0; N, 8·8. $C_{29}H_{29}O_3N_3$ requires C, 74·5; H, 6·2; N, 9·0%); and the p-*t-butylanilide* (87·8%), purified by toluene–alumina, and crystallised from toluene in bright red prisms, m. p. 209—210° (Found: C, 77·6; H, 6·6; N, 8·5. $C_{31}H_{33}O_2N_3$ requires C, 77·6; H, 6·2; N, 8·7%).

Yellow dyes: Naphtol AS-L3G (1·7 g.) gave the *dye* (I), which crystallised from chlorobenzene or mixed xylenes in yellow prisms, m. p. 286—287° (decomp.) (1·8 g., 82%) (Found: N, 9·9; Cl, 8·5. $C_{48}H_{50}O_6N_6Cl_2$ requires N, 9·6; Cl, 8·1%); Brenthol AT (1·2 g.) afforded *2,2'-bis-*(p-*t-butylphenylazoacetoacetamido*)*biphenyl*, which crystallised from chlorobenzene in yellow needles, m. p. 287—288° (decomp.) (1·5 g., 85·7%) (Found: N, 11·8. $C_{42}H_{48}O_4N_6$ requires N, 12·0%).

Brown dye: Brenthol BT (2 g.) gave 3-N-p-*chlorophenylcarbamoyl-2-hydroxy*-1-p-*t-butylphenylazocarbazole* (2·2 g., 88·6%), deep brown needles, m. p. 256—257° (from benzene) (Found: C, 70·8; H, 5·0; N, 11·5; Cl, 7·3. $C_{29}H_{23}O_2N_4Cl$ requires C, 70·1; H, 5·0; N, 11·3; Cl, 7·15%).

Azoic Dyes from 3-Hydroxy-N-p-t-butylphenyl-2-naphthamide and Diazotised Amines.—1-Naphthylamine (0·9 g.), diazotised in aqueous hydrochloric acid, and coupled with the *p*-t-butylanilide (B) (1·7 g.) in sodium hydroxide (0·8 g.), water (20 ml.), and ethanol (10 ml.) at 5°, afforded *3-hydroxy-4-1'-naphthylazo-N-p-t-butylphenyl-2-naphthamide*, which crystallised from pyridine in brownish-violet prisms with a metallic lustre, m. p. 274—275° (decomp.) (2·2 g., 92·7%) (Found: C, 78·5; H, 5·7; N, 9·2. $C_{31}H_{27}O_2N_3$ requires C, 78·6; H, 5·7; N, 8·9%).

2,5-Dichloroaniline (0·8 g.) similarly gave the *4-(2,5-dichlorophenylazo)-dye*, bright red plates (from pyridine), m. p. 287—288° (decomp.) (2·1 g., 85·3%) (Found: C, 65·5; H, 4·5; N, 8·9; Cl, 13·8. $C_{27}H_{23}O_2N_3Cl_2$ requires C, 65·8; H, 4·7; N, 8·5; Cl, 14·4%). *p*-Nitroaniline (0·7 g.) and 2-nitro-*p*-toluidine (0·75 g.) with the t-butylanilide (B) (1·7 g.), yielded, respectively, the 1-p-*nitrophenylazo-dye*, deep red needles (from acetic acid), m. p. 282—283° (decomp.) (Found: C, 69·0; H, 4·9; N, 11·7. $C_{27}H_{24}O_4N_4$ requires C, 69·2; H, 5·1; N, 11·95%), and the 1-(2-*nitro*-p-*tolylazo*)-*dye*, red needles (from pyridine) (1·9 g., 78·8%), m. p. 269—270° (decomp.) (Found: N, 11·7. $C_{28}H_{26}O_4N_4$ requires N, 11·6%), respectively.

Derivatives from o-*t-Butylaniline.*—The required calculated analyses figures for the derivatives are not repeated where the figures have been recorded above for the isomers in the *p*-t-butylaniline series.

o-t-Butylaniline [4] (C) (4 g.), b. p. 102—106°/10 mm. [acetyl derivative, colourless needles (from benzene), m. p. 161—162°], was converted as described for the *p*-t-butyl analogue into *3-hydroxy-N-o-t-butylphenyl-2-naphthamide* (A) which crystallised from ethanol in pale buff plates, m. p. 204—206° (5·2 g., 60·8%) (Found: C, 78·5; H, 6·4; N, 4·3%).

Azoic dyes. Red: N-*phenyl*, bright red prismatic needles (from acetic acid). m. p. 221—222° (70·1%) (Found: C, 75·9; H, 5·8; N, 10·1%), N-o-*tolyl*, red prisms (from acetic acid), m. p.

214° (73·4%) (Found: C, 76·4; H, 6·0; N, 10·0%), N-(4-*methoxy*-o-*tolyl*), dark red needles (from acetic acid), m. p. 210—212° (81·2%) (Found: C, 73·9; H, 6·1; N, 8·9%), and N-o-*t-butylphenyl derivative*, bright red prismatic needles (from acetic acid), m. p. 205—207° (75·6%) (Found: C, 77·2; H, 6·9; N, 8·8%), of 3-hydroxy-4-*o*-t-butylnaphthylazo-2-naphthamide.

Yellow dyes: *terephthaloylbis*-[4-*chloro*-2-*methoxy*-5-*methyl*-α-(o-*t-butylphenylazo*)*acetanilide*], bright yellow prismatic needles (from xylene), m. p. 287—289° (decomp.) (73·4%) (Found: C, 66·0; H, 5·9; N, 9·1; Cl, 8·5. $C_{48}H_{50}O_6N_6Cl_2$ requires C, 65·7; H, 5·7; N, 9·6; Cl, 8·1%), and 2,2′-*di*-(o-*t-butylphenylazoacetoacetamido*)*biphenyl*, yellow prisms (from toluene), m. p. 291—293° (decomp.) (80·4%) (Found: C, 71·5; H, 6·6; N, 12·1. $C_{42}H_{46}O_4N_6$ requires C, 72·0; H, 6·8; N, 12·0%).

Brown dye: 3-*N*-p-*chlorophenylcarbamoyl*-2-*hydroxy*-1-o-*t-butylphenylazocarbazole* crystallised from acetic acid in dark brown needles, m. p. 243—245° (72·6%) Found: C, 69·8; H, 5·1; N, 10·7; Cl, 6·8%).

Azoic Dyes from Anilide (A).—This amide gave 1-1′*naphthylazo*-, brownish-violet prismatic needles with a green lustre (from xylene), m. p. 242—243° (84·3%) (Found: C, 78·7; H, 5·5; N, 8·7%), 1-(2,5-*dichlorophenylazo*)-, bright red prismatic needles (from xylene), m. p. 263—264° (81·3%) (Found: C, 66·0; H, 4·5; N, 9·0; Cl, 15·1%), 1-p-*nitrophenylazo*-, lustrous red needles (from acetic acid), m. p. 239—240° (83·7%) (Found: C, 68·8; H, 4·8; N, 11·7%), and 1-(2-*nitro*-p-*tolylazo*)-*derivative*, dark red prisms (from acetic acid), m. p. 283—285°, (decomp.) (75%) (Found: C, 69·2; H, 5·1; N, 12·0. $C_{28}H_{26}O_4N_4$ requires C, 69·7; H, 5·3; N, 11·6%), of 3-hydroxy-*N*-*o*-t-butylphenyl-2-naphthamide.

Derivatives from m-*t-Butylaniline.*—*m*-t-Butylaniline,[5] b. p. 114—116°/13 mm. [acetyl derivative, leaflets (from ethanol), m. p. 99—101°], was converted into 3-*hydroxy*-N-m-*butylphenyl*-2-*naphthamide*, light buff-coloured plates (from ethanol), m. p. 186—188° (88%) (Found: C, 78·8; H, 6·6; N, 3·8%): the corresponding m-*toluidide* crystallised from ethanol in pale buff-coloured hexagonal plates, m. p. 210—211° (84%) (Found: C, 78·2; H, 5·6; N, 4·9%).

Azoic dyes: the o-*toluidide*, lustrous red prisms (from pyridine), m. p. 172—173° (80·7%) (Found: C, 76·5; H, 5·7; N, 9·9%), and m-*t-butylanilide*, red needles, (from toluene), m. p. 230—231° (90·7%) (Found: C, 77·6; H, 6·8; N, 8·9%), of 3-*hydroxy*-4-m-*t-butylphenylazo*-2-*naphthoic acid*; 2,2′-*bis*-(m-*t-butylphenylazoacetoacetamido*)*biphenyl*, orange-yellow needles (from pyridine), m. p. 269—270° (89%) (Found: C, 71·6; H, 6·6; N, 11·8%); and 3-N-p-*chlorophenylcarbamoyl*-2-*hydroxy*-1-m-*t-butylphenylazocarbazole*, dark brown needles with a metallic lustre (from pyridine), m. p. 249—251° (79%) (Found: C, 69·7; H, 5·4; N, 11·0; Cl, 7·5%); N-m-*t-butylphenyl*-3-*hydroxy*-4-1′-*napthylazo*-, reddish-brown needles (from pyridine), m. p. 217—218° (91%) (Found: C, 78·3; H, 5·5; N, 9·2%), and -4-p-*nitrophenylazo*-2-*naphthamide*, dark red plates (from pyridine), m. p. 245—246° (89·7%) (Found: C, 69·3; H, 5·1; N, 11·7%).

3,3′-*Di-t-butylbenzidine Dihydrochloride.*—*o*-Nitro-t-butylbenzene (12·1 g.), sodium hydroxide (14 g.), zinc powder (18 g.), water (30 ml.), and methanol (100 ml.) were refluxed with stirring for 10 hr.; the deep orange mixture became pale yellow; after rapid filtration of the hot mixture, the filtrate was kept at 0°, yielding 2,2′-*di-t-butylhydrazobenzene*, which separated in light yellow prisms, m. p. 88—91°; these were collected, washed with dilute aqueous ethanol, and dried (5 g., 50%) (Found: C, 80·7; H, 9·3; N, 9·3. $C_{20}H_{28}N_2$ requires C, 81·1; H, 9·4; N, 9·4%). The hydrazo-compound (4 g.) was dissolved in ether (15 ml.) and added gradually to a stirred solution of hydrochloric acid (7 ml.) and water (7 ml.); more hydrochloric acid (6 ml.) was added and the mixture stirred for a further hr. and then kept at 0° for 2 hr. The colourless *dihydrochloride* was deposited; a further amount separated on addition of hydrochloric acid to the filtrate: the combined material was washed with ether to remove unchanged hydrazo-derivative and dried (1·5 g., 30·6%) (Found: C, 64·9; H, 8·0; N, 7·6; Cl, 19·0. $C_{20}H_{30}N_2Cl_2$ requires C, 65·0; H, 8·1; N, 7·6; Cl, 19·2%). Tetrazotisation in dilute aqueous hydrochloric acid gave a clear solution of the bisdiazonium salt, from which the following bisazo-dyes were obtained: the *bis*-3-*hydroxy*-N-o-*tolyl*-2-*naphthamide*), dark blue rhombohedra with a yellow lustre (from pyridine), m. p. 308—310° (decomp.) (90·9%) (Found: N, 9·9. $C_{56}H_{52}O_4N_6$ requires N, 9·9%), and the 4′-*t-butyl analogue*, dark blue leaflets (from pyridine), m. p. 310—312° (decomp.) (Found: N, 9·0. $C_{62}H_{64}O_4N_6$ requires N, 8·8%).

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790. *The Stability of the* $Zn(CN)_4^{2-}$ *Ion.*

By M. S. Blackie and V. Gold.

The equilibrium constant for the reaction $Zn(CN)_4^{2-} \rightleftharpoons Zn^{2+} + 4CN^-$ at 25° has been re-determined by an e.m.f. method. The value found is $1{\cdot}9_1 \times 10^{-17}$ mole^4 l.$^{-4}$.

The equilibrium constant for the reaction

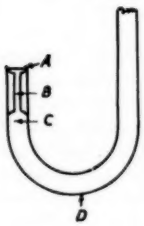
$$Zn(CN)_4^{2-} \rightleftharpoons Zn^{2+} + 4CN^- \quad \ldots\ldots\ldots\ldots \quad (I)$$

was first determined electrometrically by Euler,[1] who obtained the value $1{\cdot}3 \times 10^{-17}$ mole^4 l.$^{-4}$. More recent determinations [2] have given values ranging from $2{\cdot}5 \times 10^{-13}$ to *ca.* 10^{-20}, the former extreme being a recent Russian result [3] and the latter the limit of a range of values obtained by Britton and Dodd [4] in 1932. Latimer's free-energy values [5] are consistent with a value of 1×10^{-17}. In view of the discrepancies, the determination has been repeated by the use of e.m.f. measurements, as in Euler's original work. One half-cell contained a zinc electrode in contact with a 0·01M-solution of zinc sulphate, and the other half-cell an identical electrode with a solution of zinc sulphate containing an excess of added potassium cyanide. For reasons of experimental convenience, the two half-cells were connected through a salt bridge specially designed to afford both easy assembly and the desirable [6] cylindrical symmetry of the junctions. The presence of liquid junctions in the cell nevertheless imposes certain limitations on the significance of the procedure.

Experimental.—The cell

$$Zn \mid ZnSO_4 \text{ aq.} \mid KCl \text{ aq.} \mid ZnSO_4 + KCN \text{ aq.} \mid Zn$$
$$c_1 = 0{\cdot}01\text{M} \quad 3{\cdot}5\text{M} \quad c_2 = z\text{M} \quad 8z\text{M}$$

was set up, electrodes of spectroscopically pure zinc being used. Other chemicals were analytical reagents. E.m.f.s were measured at 25·00° ± 0·05° on a Cambridge Vernier potentiometer.



A detail of the construction of the salt bridge and method of forming liquid junctions are shown in the Figure. The open end *A* of the salt bridge was below the level of liquid in the half-cell. The main part of the tube (*D*) was filled with 3·5M-potassium chloride set in 3% aqueous agar-agar. The portion *B*–*C* was filled with aqueous 3·5M-potassium chloride, and zinc solution (of the same composition as that in the half-cell) was then carefully added to fill the portion *A*–*B*. The liquid junction was thus formed as a kind of free-diffusion junction in the narrow part of the tube at *B*. The portion *A*–*C* was emptied and washed out on changing solutions in the half-cell.

Discussion

The e.m.f. of the cell considered is given by

$$E = (\boldsymbol{R}T/2\boldsymbol{F}) \ln (a_2/a_1) + \Delta\pi_j$$

where a_1 and a_2 are the activities of zinc ions in the two half-cells and $\Delta\pi_j$ is the residual liquid-junction potential. In view of the low ionic concentrations in the half-cells, compared with that in the salt bridge, we shall assume that $\Delta\pi_j$ may be set equal to zero in the following calculation. We shall also assume that the single-ion activities a_1 and a_2 may be

[1] Euler, *Ber.*, 1903, **36**, 3400.
[2] "Stability Constants. Part II: Inorganic Ligands," Chem. Soc. Special Publ. No. 7 (1958).
[3] Stabrovskii, *Zhur. obshchei Khim.*, 1951, **21**, 1223.
[4] Britton and Dodd, *J.*, 1932, 1940.
[5] Latimer, "The Oxidation States of the Elements and their Potentials in Aqueous Solution," 2nd edn., Prentice-Hall Inc., New York, 1952.
[6] Guggenheim, *J. Amer. Chem. Soc.*, 1930, **52**, 1315.

equated to the mean activity of zinc sulphate, an assumption that is more justifiable at low than at high ionic strengths. The reference half-cell always contained 0·01M-zinc sulphate, the mean activity of which [7] is 0·00387M.

The following equilibria have been considered together with (1), in connection with the problem:

$$CN^- + H_2O \rightleftharpoons HCN + OH^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$$ZnOH^+ \rightleftharpoons Zn^{2+} + OH^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

The equilibrium constant of (1), K_1, is the required quantity. The basicity constant of cyanide ion (in terms of activities), $K_2 = (HCN)(OH^-)/(CN^-)$, is identical with the ratio K_w/K_A where K_w is the ionic product of water and K_A the acid dissociation constant of hydrocyanic acid. K_2 was calculated from tables of standard Gibbs free energies of formation [8] to have the value $2{\cdot}434 \times 10^{-5}$. The formation of $ZnOH^+$ and reaction (3) will be neglected in the following two paragraphs. Their rôle is briefly considered thereafter.

The thermodynamic equilibrium constant for (1) is defined in terms of activities by

$$K_1 = (Zn^{2+})(CN^-)^4/(Zn(CN)_4^{2-})$$

It is convenient also to define the auxiliary function K_1''

$$K_1'' = (Zn^{2+})[CN^-]^4/[Zn(CN)_4^{2-}]$$

where square and round brackets signify concentrations and activities respectively. The ratio K_1/K_1'' is identical with the activity coefficient ratio $\gamma^4_{CN^-}/\gamma_{Zn(CN)_4^{2-}}$ which is unity in the range of applicability of the Debye–Hückel limiting law for 1 : 1- and 2 : 1-electrolytes.

Assuming this law for 1 : 1-electrolytes, we may replace the thermodynamic constant K_2 by the corresponding classical constant K_2', where $K_2/K_2' = \gamma_{OH^-}\gamma_{HCN}/\gamma_{CN^-}$. The concentrations of CN^- and $Zn(CN)_4^{2-}$ ions are calculated from the relations

$$[Zn(CN)_4^{2-}] = [Zn^{2+}]_{stoich.} - [Zn^{2+}]; \; [CN^-] = [CN^-]_{stoich.} - 4[Zn(CN_4^{2-}] - [HCN]$$

$$K_2' = [HCN]^2/[CN^-]$$

The activity of zinc ions, a_2, is obtained from the e.m.f. measurements on the basis of the assumptions stated in the first paragraph of the Discussion. Combining this activity with the concentration ratio $[CN^-]^4/[Zn(CN)_4^{2-}]$, we obtain K_1''. A summary of results and calculations is given in the Table.

Table of results.

$[Zn^{2+}]_{stoich.}$	$[CN^-]_{stoich.}$	E (v)	(Zn^{2+}) *	$[Zn(CN)_4]^{2-}$	$[CN^-]$	Ionic strength	$10^{17}\,K_1''$
10^{-2}	8×10^{-2}	0·3148	$8{\cdot}96 \times 10^{-14}$	10^{-2}	$3{\cdot}903 \times 10^{-2}$	10^{-1}	2·08
5×10^{-3}	4×10^{-2}	0·2882	$6{\cdot}98 \times 10^{-13}$	5×10^{-3}	$1{\cdot}932 \times 10^{-2}$	5×10^{-2}	1·94
10^{-3}	8×10^{-3}	0·2242	$1{\cdot}022 \times 10^{-10}$	10^{-3}	$3{\cdot}701 \times 10^{-3}$	10^{-2}	1·92
5×10^{-4}	4×10^{-3}	0·1958	$9{\cdot}49 \times 10^{-10}$	5×10^{-4}	$1{\cdot}792 \times 10^{-3}$	5×10^{-3}	1·91
10^{-4}	8×10^{-4}	0·1270	$1{\cdot}98 \times 10^{-7}$	$9{\cdot}93 \times 10^{-5}$	$3{\cdot}152 \times 10^{-4}$	10^{-3}	1·96 †
5×10^{-5}	4×10^{-4}	0·0951	$2{\cdot}33 \times 10^{-6}$	—	—	5×10^{-4}	—

* $(Zn^{2+}) = \dfrac{0{\cdot}00387}{\text{antilog}\,(2E/0{\cdot}05916)}$.

† Calculated by assuming $K_3'' = 4 \times 10^{-5}$. Neglecting association, we find $K_1'' = 1{\cdot}91 \times 10^{-17}$.

The presence of hydroxide ions in solution from the hydrolysis of cyanide raises the possibility of the formation of $ZnOH^+$ by the reverse of reaction (3). The classical equilibrium constant $K'_3 = [Zn^{2+}][OH^-]/[ZnOH^+]$ has been the subject of several investigations but its value is still in considerable doubt. Davies,[9] basing his conclusions on

[7] Cowperthwaite and La Mer, *J. Amer. Chem. Soc.*, 1931, **53**, 4333.

[8] "Selected values of Chemical Thermodynamic Properties" (N.B.S. Circular 500, U.S. Dept. of Commerce, Washington, D.C., 1952).

[9] Davies, *J.*, 1951, 1256.

experimental work by Owen and Gurry [10] and by Kolthoff and Kameda,[11] finds a value of 4×10^{-5}. Earlier investigations [2] had given much lower values, whereas one more recent study [12] gives the higher value $1{\cdot}6 \times 10^{-4}$. A much lower result (2×10^{-6}) has also recently been reported.[13]

In principle, the association can be entirely allowed for by solving the five simultaneous equations (which may also be expressed in different forms)

$$[Zn^{2+}]_{stoich.} = [Zn(CN)_4^{2-}] + [Zn^{2+}] + [ZnOH^-]$$
$$[CN^-]_{stoich.} = [CN^-] + 4\,[Zn(CN)_4^{2-}] + [HCN]$$
$$[HCN] = [OH^-] + [ZnOH^+]$$
$$K_2' = [OH^-][HCN]/[CN^-]$$
$$K_3'' = (Zn^{2+})[OH^-]/[ZnOH^+]$$

for the relevant concentrations. Using this procedure we find that the concentration of $[ZnOH^+]$ is entirely negligible except for the two most dilute solutions. For the penultimate solution, consideration of the association results in a small correction which is barely outside the limits of experimental accuracy of the value of K_1''. For the most dilute solution the effect of association is large and, in view of the uncertainty in the value of K_3, a reliable value of K_1'' cannot be calculated for this point.

It was pointed out at the beginning of the Discussion that K_1'' should not differ from K_1 in the range of applicability of the Debye–Hückel limiting law. Accordingly, it is expected that K_1'' should approach K_1 and constancy as the ionic strength decreases to zero. This trend towards constancy is found.

The fairly close agreement of our value with Euler's is largely fortuitous, since *inter alia* Euler did not consider hydrolysis of cyanide ion. Our procedure is subject to the uncertainty inherent in the assumption of complete elimination of liquid-junction potentials by the use of a salt bridge. However, it seems that the largest source of error in the calculated results lies in the assumed values for the activity coefficient of 0·01M-zinc sulphate and for the acid dissociation constant of hydrocyanic acid.

KING'S COLLEGE, STRAND, LONDON, W.C.2. [*Received, April 17th*, 1959.]

[10] Owen and Gurry, *J. Amer. Chem. Soc.*, 1938, **60**, 3074.
[11] Kolthoff and Kameda, *J. Amer. Chem. Soc.*, 1931, **53**, 832.
[12] Brown and Cranston, *J.*, 1940, 578.
[13] Schwab and Polydoropoulos, *Z. phys. Chem.*, 1953, **274**, 234.

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791. *Thermodynamics of Ion Association. Part VI.*[1] *Some Transition-metal Sulphates.*

By V. S. K. NAIR and G. H. NANCOLLAS.

E.m.f.s of cells of the type H_2,Pt|MSO_4,HCl|AgCl|Ag have been measured by a precision method at temperatures from 0° to 45° and thermodynamic association constants are derived for the formation of $MnSO_4$, $CoSO_4$, and $NiSO_4$. ΔH, ΔG, and ΔS are evaluated for the reaction $M^{2+} + SO_4^{2-} \rightleftharpoons MSO_4$, and these are discussed.

THE stability of transition-metal complexes has been discussed by Irving and Williams [2] who found that for a number of neutral ligands and anions of weak acids, the association constants lie in the sequence Mn < Fe < Co < Ni < Cu > Zn. Owing to the lack of temperature-coefficient data, however, all such discussions involve the assumption that the free-energy change is dominated by the heat term and that changes in the entropy of

[1] Part V, Nair and Nancollas, *J.*, 1958, 4144.
[2] Irving and Williams, *J.*, 1953, 3192.

association may be neglected. Both the heat and the entropy term should be considered, and the present investigation extends the available data for sulphates [3] to those of manganese, cobalt, and nickel. Cells of the type described previously [1,3]

$$H_2,Pt \mid HCl,MSO_4 \mid AgCl \mid Ag$$

have been used, and e.m.f.s have been measured at various temperatures between 0° and 45°.

Experimental

"AnalaR" manganese, cobalt, and nickel sulphates were recrystallised three times from conductivity water. Manganese sulphate has a maximum solubility at 54—55° and solutions prepared at this temperature were evaporated to about two-thirds of the original volume before crystallisation. Recrystallised manganese and cobalt sulphates were converted into the anhydrous forms and stock solutions were prepared as described previously:[3] analysis for sulphate by precipitation as barium sulphate agreed to within 0·03% of the calculated concentrations. Since anhydrous nickel sulphate dissolves in water only with difficulty, stock solutions were prepared from the hydrated salt and analysed for nickel by precipitation as the dimethylglyoxime.[4] Duplicated estimations agreed to 0·02%. The apparatus and experimental technique have been described previously.[1] E.m.f. readings were constant to within 20 μv.

Results and Discussion

The concentration of hydrogen ions, m_{H^+}, in the cell

$$H_2,Pt \mid HCl(m_1), MSO_4(m_2) \mid AgCl \mid Ag$$

can be expressed by

$$-\log m_{H^+} = (E - E^\circ)/k + \log m_1 + \log \gamma_{H^+}\gamma_{Cl^-}$$

where γ represents activity coefficient, m molalities, and $k = 2{\cdot}3026\ RT/F$. Using equations for the concentrations of ionic species: $m_{HSO_4^-} = m_1 - m_{H^+}$, $m_{M^{2+}} = m_{HSO_4^+} + m_{SO_4^{2-}}$, and $m_{MSO_4} = m_2 - m_{M^{2+}}$, and the dissociation constant of the bisulphate ion, $k_2 = a_{H^+}a_{SO_4^{2-}}/a_{HSO_4^-}$, we calculated the thermodynamic association constants $K = a_{MSO_4}/a_{M^{2+}}a_{SO_4^{2-}}$ by the method described previously.[3] Activity coefficients were obtained from Davies's modification of the Debye–Hückel equation [5]

$$\log \gamma_z = Az^2[I^{\frac{1}{2}}/(1 + I^{\frac{1}{2}}) - CI]$$

in which $C = 0{\cdot}2$. The results are summarized in Table 1 which includes the mean values of K at each temperature.

The association constants at 25°, $K(CoSO_4) = 230$ kg. mole^{-1} and $K(NiSO_4) = 211$ kg. mole^{-1}, are lower than the corresponding values 294 and 250 obtained by Money and Davies [6] from conductivity measurements: for manganese sulphate, however, our value, 181 kg. mole^{-1} is in good agreement with James's conductimetric value,[7] 192 kg. mole^{-1}. At 0°, $K(NiSO_4) = 121$ kg. mole^{-1} and $K(CoSO_4) = 172$ kg. mole^{-1} can be compared with the cryoscopic values, 125 and 111 respectively, obtained by Brown and Prue.[8] The $CoSO_4$ values are rather different and it is noteworthy that the cryoscopic results show small systematic deviations for all the curves in the case of cobalt sulphate.[8]

Heats of association have been derived by use of least squares from the linear plots of log K against T^{-1} shown in the Figure. Values of ΔG, ΔH, and ΔS together with mean deviations (calculated by least squares on the assumption that the deviations of the points from the straight lines in the Figure are themselves a measure of the error in ΔH), are

[3] Nair and Nancollas, Part IV, *J.*, 1958, 3706.
[4] Vogel, "A Text Book of Quantitative Analysis," Longmans, London, 1947.
[5] Davies, *J.*, 1938, 2093.
[6] Money and Davies, *Trans. Faraday Soc.*, 1932, **28**, 609.
[7] James, Ph.D. Thesis, London, 1947.
[8] Brown and Prue, *Proc. Roy. Soc.*, 1955, *A*, **232**, 320.

TABLE 1. *E.m.f. measurements.*

Manganese sulphate

	Expt.		1	2	3	4	5	
	10^3m_1		3·777	6·122	8·679	3·903	2·824	
	10^3m_2		2·648	5·334	4·425	7·254	12·948	
Temp.	Expt.	$(E - E^\circ)$	10^3I	$10^3m_{HSO_4^-}$	$10^3m_{M^{2+}}$	$10^3m_{MSO_4}$	K	K (mean)
0°	2	0·24873	23·95	0·504	4·707	0·627	101	
	1	0·26916	13·15	0·194	2·423	0·225	103	
	3	0·23188	23·48	0·590	3·992	0·433	101	103
	4	0·27099	27·98	0·415	6·205	1·049	101	
	5	0·28891	43·53	0·435	10·409	2·539	107	
10°	1	0·27947	12·75	0·256	6·205	1·049	135	
	2	0·25853	23·21	0·651	10·409	2·539	129	
	3	0·24097	22·97	0·761	2·373	0·275	122	129
	4	0·28185	27·13	0·539	4·602	0·732	123	
	5	0·30077	41·75	0·555	3·945	0·480	134	
20°	1	0·29004	12·53	0·346	2·350	0·298	158	
	2	0·26863	22·43	0·852	4·505	0·839	165	
	3	0·25024	22·22	0·988	3·884	0·541	154	160
	4	0·29306	25·97	0·704	5·858	1·396	161	
	5	0·31331	40·21	0·720	9·734	3·214	161	
25°	1	0·29526	12·32	0·381	2·329	0·319	176	
	2	0·27359	22·10	0·927	4·455	0·879	181	
	3	0·25457	21·90	1·069	3·839	0·586	178	181
	4	0·29859	25·47	0·767	5·776	1·478	178	
	5	0·31919	38·79	0·770	9·372	3·576	193	
35°	1	0·30593	11·97	0·473	2·287	0·361	218	
	2	0·28391	21·54	1·136	4·427	0·907	204	
	3	0·26417	21·32	1·288	3·799	0·626	214	212
	4	0·31014	24·74	0·937	5·668	1·586	208	
	5	0·33217	37·63	0·932	9·192	3·756	218	
45°	1	0·31672	11·60	0·511	2·240	0·408	276	
	2	0·29427	20·68	1·333	4·307	1·037	265	
	3	0·27361	20·64	1·503	3·739	0·686	269	262
	4	0·32193	23·83	1·112	5·528	1·726	250	
	5	0·34552	36·56	1·094	8·975	3·973	251	

Cobalt sulphate

	Expt.		1	2	3	4	5	6	
	10^3m_1		6·933	5·960	8·259	6·986	4·488	5·865	
	10^3m_2		4·177	3·360	6·079	7·369	4·061	5·850	
Temp.	Expt.	$(E - E^\circ)$	10^3I	$10^3m_{HSO_4^-}$	$10^3m_{M^{2+}}$	$10^3m_{MSO_4}$	K	K (mean)	
0°	1	0·24193	20·12	0·444	3·522	0·655	178		
	2	0·24842	16·96	0·336	2·923	0·437	158		
	3	0·23494	26·75	0·675	4·958	1·121	179		
	4	0·24356	29·37	0·666	5·908	1·461	170	172	
	5	0·26209	17·46	0·298	3·399	0·662	172		
	6	0·25076	23·86	0·489	4·746	1·104	174		
5°	1	0·24657	19·95	0·491	3·516	0·661	184		
	2	0·25314	16·77	0·369	2·890	0·470	177		
	3	0·23949	26·46	0·741	4·926	1·153	190		
	4	0·24818	28·82	0·733	5·820	1·549	185	185	
	5	0·26710	17·27	0·329	3·370	0·691	188		
	6	0·25559	23·61	0·532	4·700	1·150	188		
15°	1	0·25628	19·65	0·658	3·509	0·668	200		
	2	0·26286	16·42	0·496	2·865	0·495	202		
	3	0·24899	25·98	0·988	4·934	1·145	201		
	4	0·25816	28·29	0·981	5·822	1·547	196	200	
	5	0·27750	17·05	0·448	3·365	0·696	200		
	6	0·26573	23·13	0·721	4·678	1·172	205		
25°	1	0·26587	19·18	0·842	3·484	0·480	228		
	2	0·27283	16·06	0·640	2·850	0·510	226		
	3	0·25862	25·26	1·245	4·872	1·207	237		
	4	0·26831	27·52	1·236	5·726	1·643	231	230	
	5	0·28815	16·91	0·590	3·403	0·658	(196)		
	6	0·27633	22·60	0·925	4·644	1·206	229		

TABLE 1. (*Continued.*)

Cobalt sulphate (contd.)

Temp.	Expt.	$(E - E^\circ)$	10^3I	$10^3m_{HSO_4^-}$	$10^3m_{M^{2+}}$	$10^3m_{MSO_4}$	K	K (mean)
35°	1	0·27569	18·74	1·033	3·478	0·699	250	
	2	0·28267	15·70	0·786	2·829	0·531	260	
	3	0·26837	24·71	1·520	4·877	1·202	255	
	4	0·27869	26·90	1·512	5·735	1·634	247	253
	5	0·29875	16·31	0·720	3·309	0·752	253	
	6	0·28655	22·10	1·135	4·626	1·224	251	
45°	1	0·28571	18·40	1·237	3·490	0·687	271	
	2	0·29280	15·37	0·950	2·836	0·524	279	
	3	0·27839	24·19	1·793	4·876	1·203	284	
	4	0·28937	26·43	1·805	5·768	1·601	261	277
	5	0·30961	15·88	0·870	3·282	0·779	284	
	6	0·29722	21·56	1·352	4·586	1·264	286	

Nickel sulphate

Expt.	1	2	3	4	5	6	7	8
10^3m_1	6·469	5·356	4·545	2·771	3·252	6·096	4·866	10·656
10^3m_2	2·868	2·670	1·863	5·559	9·700	11·300	4·581	3·957

Temp.	Expt.	$(E - E^\circ)$	10^3I	$10^3m_{HSO_4^-}$	$10^3m_{M^{2+}}$	$10^3m_{MSO_4}$	K	K (mean)
0°	1	0·24430	16·24	0·325	2·597	0·271	123	
	2	0·25289	14·52	0·263	2·430	0·240	117	
	3	0·25972	11·14	0·171	1·729	0·134	115	
	5	0·28069	33·64	0·413	7·833	1·867	122	121
	6	0·25187	40·63	0·810	9·040	2·260	128	
	7	0·25885	20·07	0·363	3·986	0·595	122	
10°	1	0·25369	15·85	0·421	2·552	0·316	157	
	2	0·26257	14·18	0·344	2·386	0·284	150	151
	3	0·26959	10·90	0·226	1·705	0·158	146	
15°	1	0·25840	15·64	0·477	2·533	0·335	174	
	2	0·26746	14·00	0·388	2·358	0·312	174	
	3	0·27454	10·78	0·256	1·687	0·176	170	
	4	0·30275	19·93	0·593	4·470	1·089	179	174
	5	0·29776	31·73	0·593	7·418	2·282	172	
	6	0·26737	38·23	1·148	8·617	2·683	176	
	7	0·27408	19·20	0·532	3·848	0·733	171	
25°	1	0·26797	15·20	0·606	2·480	0·388	228	
	2	0·27741	13·75	0·502	2·341	0·329	200	
	3	0·28460	10·57	0·335	1·677	0·186	195	
	4	0·31442	19·22	0·467	4·344	1·215	219	
	5	0·30968	30·52	0·750	7·183	2·517	208	211
	6	0·27828	37·04	1·437	8·437	2·863	207	
	7	0·28452	18·59	0·682	3·772	0·809	207	
	8	0·24321	17·94	1·133	3·373	0·584	227	
35°	1	0·27765	14·87	0·745	2·471	0·397	256	
	2	0·28737	13·37	0·620	2·313	0·357	239	
	3	0·29469	10·32	0·415	1·651	0·212	246	
	4	0·32636	18·73	0·580	4·278	1·281	247	247
	5	0·32190	29·54	0·912	7·026	2·674	239	
	6	0·28929	35·55	1·721	8·221	3·079	247	
	7	0·29488	17·94	0·832	3·686	0·895	256	
45°	1	0·28739	14·45	0·883	2·435	0·433	310	
	2	0·29754	13·06	0·746	2·301	0·369	274	
	3	0·30494	10·11	0·505	1·645	0·218	279	
	4	0·33857	18·19	0·701	4·206	1·353	284	289
	5	0·33430	28·24	1·072	6·769	2·931	294	
	6	0·30070	34·43	2·022	8·099	3·201	280	
	7	0·30581	17·35	0·994	3·622	0·959	305	

given in Table 2; data for the sulphates of magnesium, zinc,[3] and calcium [9] are included for comparison.

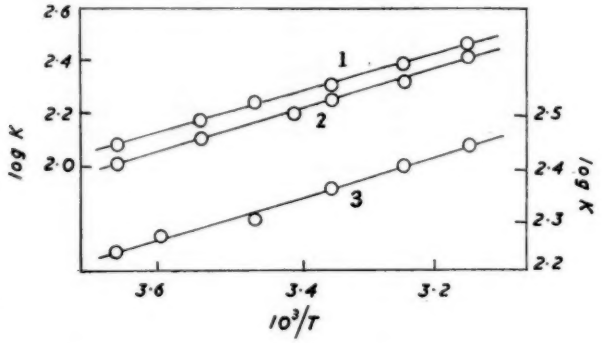
The entropy of association can be written in terms of gas and hydration entropies:

$$\Delta S = \Delta S_g + \Delta S_{hyd}(MSO_4) - \Delta S_{hyd}(M^{2+}) - \Delta S_{hyd}(SO_4^{2-})$$

[9] Bell and George, *Trans. Faraday Soc.*, 1953, **49**, 619.

There is considerable uncertainty in the value for the standard entropy of the nickel ion. Latimer [10] quotes the Bureau of Standards' value, −38·1 cal. deg.$^{-1}$ mole^{-1}, but points out that such a low value cannot be accepted in comparison with $S°(Fe^{2+})$ and $S°(Cu^{2+})$ even though there may be considerable divergence in the multiplicity of the ground states.

Plots of log K *against* T^{-1} *for* (1) *nickel sulphate*, (2) *manganese sulphate* (*left-hand ordinates*), *and* (3) *cobalt sulphate* (*right-hand ordinate*).



Staveley and Randall [11] consider −23 cal. deg.$^{-1}$ mole^{-1} to be more reliable and we have used the latter value together with −22 cal. deg.$^{-1}$ mole^{-1} for the standard entropy of the cobalt ion.[11] $\Delta S_{hyd}(MSO_4)$, calculated as described previously,[3] is given in Table 3.

TABLE 2. *Thermodynamic properties.*

Reaction	ΔH (kcal. mole^{-1})	ΔG_{298} (kcal. mole^{-1})	ΔS cal. deg.$^{-1}$ mole^{-1})
$Mn^{2+} + SO_4^{2-}$	3·37 ± 0·31	−3·07 ± 0·02	22·6 ± 1·0
$Co^{2+} + SO_4^{2-}$	1·74 ± 0·16	−3·21 ± 0·02	16·6 ± 0·5
$Ni^{2+} + SO_4^{2-}$	3·31 ± 0·20	−3·16 ± 0·03	21·7 ± 0·7
$Zn^{2+} + SO_4^{2-}$	4·01 ± 0·55	−3·25 ± 0·02	24·4 ± 1·8
$Mg^{2+} + SO_4^{2-}$	4·84 ± 0·40	−3·07 ± 0·03	26·2 ± 1·3
$Ca^{2+} + SO_4^{2-}$	1·65 ± 0·20	−3·15 ± 0·03	16·1 ± 0·8

TABLE 3. *Thermodynamic properties.*

Ion pair	S_g (MSO_4) (cal. deg.$^{-1}$ mole^{-1})	ΔS (cal. deg.$^{-1}$ mole^{-1})	$S°(MSO_4)$ (cal. deg.$^{-1}$ mole^{-1})	$-\Delta S_{hyd}$ (MSO_4) (cal. deg.$^{-1}$ mole^{-1})	r_+^{-1} (Å^{-1})
$MnSO_4$	70·1	22·6	6·7	63·4	1·28
$CoSO_4$	70·2	16·6	−1	71	1·35
$NiSO_4$	70·2	21·7	3	67	1·37
$ZnSO_4$	70·3	24·4	3·0	67·3	1·39
$MgSO_4$	68·2	26·2	2·1	66·1	1·52
$CaSO_4$	69·5	16·1	7·0	62·5	1·01

An attempt to correlate the thermodynamic data with various properties of the metal ions such as electronegativity and ionization potential showed no obvious relationship. The Irving–Williams order of stability [2] observed with a large number of neutral ligands and anions of weak acids, will be expected to hold only when the ligands interact with protons more strongly than does water. The association constants for the sulphate ion pairs are closely similar and the proton complex with this ligand is less stable than the H_3O^+ ion. Indeed, with cobalt and nickel sulphates, the Irving–Williams order is reversed.

The most frequently applied correlation involves the entropy of association and some function of the radii of the ions. It is important in this connection to consider, if possible,

[10] Latimer, "Oxidation Potentials," Prentice-Hall, New York, 1952.
[11] Staveley and Randall, *Discuss. Faraday Soc.*, 1958, **26**, 157.

only the hydration entropies of the complex ions when applying these methods since, in general, complex ions will contain different translational and rotational terms. Also the variable $\Delta S_{hyd}(M^{2+})$ term should be eliminated since this itself varies linearly with r_+^{-1}. Inspection of Table 3 indicates that there is a general increase in $-\Delta S_{hyd}(MSO_4)$ with r_+^{-1} in going from manganese to nickel and zinc but the value for cobalt appears to be anomalous. Until more reliable estimates are available for the standard entropies of nickel and cobalt ions, it is not possible to carry the comparison any further.

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792. *Intermediates in Aralkyl Systems. Part II.* Kinetics and Mechanism of Substitution of Diphenylmethyl Bromide by Anionic Reagents in Nitromethane.*

By Y. POCKER.

The reactions of tetraethylammonium bromide, chloride, and azide with diphenylmethyl bromide were investigated in nitromethane. The rates are analysed in terms of concurrent first- and second-order processes. The kinetics of the first-order component embody three features: (*a*) the initial rates of the various substitutions are practically the same, (*b*) the ionic-strength effects are similar and positive, and (*c*) in the non-symmetric substitution by chloride ions, common ions seem to be able to depress the entire first-order component. The kinetics of the second-order components are subject to a negative salt effect. It is suggested that the first- and second-order components represent a uni- and a bi-molecular substitution process respectively.

FOR the more detailed investigation of non-solvolytic unimolecular substitutions, S_N1, it is advantageous to cut out simultaneous solvolyses. A solvent must be used which sufficiently ionises the substrate to promote the desired type of substitution, but is insufficiently nucleophilic to be decomposed by the carbonium ion formed. Nitromethane partially satisfies these demands. Although it is not entirely inert towards a relatively high concentration of carbonium ions, whether added in bulk [1] or present in thermodynamic equilibrium with the substrate,[2] it is sufficiently unreactive towards alkyl halides for which the ionisation process is rate-determining.[3a,b,4] Diphenylmethyl bromide suggested itself as an aralkyl halide free from elimination reactions and at the same time likely to exhibit in nitromethane, at least in part, a unimolecular mechanism of substitution.

Our first purpose was to test how far it is necessary, without invoking stereochemistry,[5] to elaborate the S_N1 ionisation scheme in nitromethane to include a partly heterolysed but undissociated intermediate. Our second was to examine under non-solvolytic conditions in a sufficiently polar medium whether, by increasing the concentration or the nucleophilic power of the anionic substituting agent, a behaviour intermediate between

* The paper "The Ionisation of Triphenylmethyl Chloride in Nitromethane," *J.*, 1958, 240, is regarded as Part I in this Series.

[1] Burton and Cheesman, *J.*, 1953, 832.
[2] Pocker, *J.*, 1958, 240.
[3] (*a*) Gelles, Hughes, and Ingold, *J.*, 1954, 2924; (*b*) de la Mare, Hughes, Ingold, and Pocker, *ibid.*, p. 2930.
[4] Pocker, *J.*, 1959, 1179.
[5] Pocker, "Kinetics and Mechanisms of Exchange and Racemisation in Aralphyl Halides," paper presented at the Informal Faraday Soc. meeting on Isotopic Exchange Reactions in Leeds, 26th Sept., 1958. Abstracts appear in *Trans. Faraday Soc.*, 1959, **55**, 1266.

S_N1 and S_N2 would be induced (*i.e.*, borderline mechanism), or whether two concurrent and independent processes would occur.[6a-i]

(1) *Reaction of Diphenylmethyl Bromide with Bromide ions.*—Bromide ions were supplied as tetraethylammonium bromide labelled with radiobromine, ^{82}Br, of half-life 36 hr. The rate of isotopic exchange was studied over a range of reagent concentrations. The first-order rate coefficients of exchange, k_E, are given in Table 1. They were calculated

TABLE 1. *First-order rate coefficients, k_E (sec.$^{-1}$), of exchange between diphenylmethyl bromide and isotopically labelled bromide ions in nitromethane at 25·0°.*

(*a*) 10^3[Ph_2CHBr] ...	2·0	2·0	2·0	2·0	2·0	0·2	1·0	4·0			
10^3[$NEt_4{}^{82}Br$] ...	0·1	0·2	0·5	1·0	2·0	0·2	1·0	1·0			
10^5k_E	1·93	2·08	2·65	3·60	5·35	2·06	3·65	3·5			
(*b*) 10^3[Ph_2CHBr] ...	2·0	2·0	2·0	2·0	2·0	2·0	10^3[Ph_2CHBr]	2·0	2·0	2·0	
10^3[$NEt_4{}^{82}Br$] ...	0·2	0·2	0·2	0·2	0·2	0·2	10^3[$NEt_4{}^{82}Br$]	0·1	0·1	0·1	
10^3[NEt_4ClO_4] ...	0·3	0·8	1·8	2·8	5·8	3·8	10^2[NEt_4ClO_4]	1·9	2·9	5·9	
10^5k_{obs}	2·16	2·20	2·30	2·36	2·64	2·47	10^5k_E	2·13	2·18	2·44	
μ	0·005	0·010	0·020	0·030	0·060	0·040	μ	0·020	0·030	0·060	
$10^5k_1{}^\mu$	1·80 *	1·84 *	1·94 *	2·00 *	2·28 *	2·11 *	$10^5k_1{}^\mu$	1·95 †	2·00 †	2·26 †	

* Calculated from k_{obs} by using k_2[NEt_4Br] = 0·36 × 10^{-5} sec.$^{-1}$.
† Calculated from k_{obs} by using k_2[NEt_4Br] = 0·18 × 10^{-5} sec.$^{-1}$.

(*c*) 10^3[Ph_2CHBr]	2·0	2·0	2·0	2·0
10^3[$NEt_4{}^{82}Br$]	2·0	2·0	2·0	2·0
10^3[NEt_4ClO_4]	—	1·0	2·0	4·0
10^5k_E	5·35	5·30	5·26	5·16

by a method (Experimental) which allows for radioactive decay and dilution and for any reaction which occurs during mixing. The results indicate that the rate of exchange, v_E, is best expressed by the equation:

$$v_E = k_E[Ph_2CHBr] = k_1[Ph_2CHBr] + k_2[Ph_2CHBr][NEt_4Br]$$

where at low ionic strength $10^5k_1 = 1·75 \pm 0·05$ sec.$^{-1}$ and $10^5k_2 = 180 \pm 5$ sec.$^{-1}$ l. mole^{-1}. To obtain the dependence of k_1 on the ionic strength, the effect of added tetraethylammonium perchlorate was investigated in detail (Table 1*b*). When [NEt_4Br] = 0·002M, the contribution of the second-order component, k_2[Ph_2CHBr][NEt_4Br] is only 15% of the overall rate of exchange, so that variations in k_{obs} can be analysed as being mainly due to variations in k_1. This analysis is confirmed by the more limited range of results obtained with [NEt_4Br] = 0·001M, where the second-order component is only 7·5% of the overall rate of exchange. At higher concentrations of saline bromide the dependence of k_{obs} on the ionic strength (Table 1*c*) is such as to suggest that k_2 itself is subject to a negative salt effect as would accord with its being a rate coefficient of a bimolecular S_N2 reaction between a neutral molecule and an anion.

The stabilisation effect by means of an ionic atmosphere of the transition state of the unimolecular component can to a first approximation be expressed [7] by

$$\log (k_1{}^\mu/k_1{}^0) = (0·912 \times 10^{16})\sigma\mu/(DT)^2$$

where $k_1{}^\mu$ is the first-order rate coefficient of ionisation in a solution of ionic strength μ and $k_2{}^0$ is the limiting value as the ionic strength approaches zero. The logarithmic ratio depends on the ionising molecule through a parameter σ of the transition state, the dielectric constant (D = 36 at 25·0°), and absolute temperature (T = 298°). This is a

[6] (*a*) Gleave, Hughes, and Ingold, *J.*, 1935, 236; (*b*) Baker and Nathan, *J.*, 1935, 1842; (*c*) Hughes, Ingold, and Shapiro, *ibid.*, 1936, 228; (*d*) Baker, *Trans. Faraday Soc.*, 1941, **37**, 632; (*e*) Winstein, Grunwald, and Jones, *J. Amer. Chem. Soc.*, 1951, **73**, 2700; (*f*) Swain and Langsdorf, jun., *ibid.*, p. 2813; (*g*) Dewar, *Ann. Reports*, 1951, **48**, 118; (*h*) Bird, Hughes, and Ingold, *J.*, 1954, 634; (*k*) Gold, *ibid.*, 1956, 4633; (*l*) Kohnstam, Queen, and Shillaker, *Proc. Chem. Soc.*, 1959, 158.

[7] Bateman, Church, Hughes, Ingold, and Taher, *J.*, 1940, 979.

limiting law for dilute solutions where the dissociation of the saline species is practically complete. It follows from the above equation that a plot of log k_1^{μ} against μ ($= [NEt_4ClO_4] + [NEt_4Br]$) should be linear with intercept log k_1^0 and slope $0{\cdot}788 \times 10^8$. From the slope, using the data for k_1^{μ} given in Table 1*b*, one obtains $\sigma = 2{\cdot}45 \times 10^{-8}$. If we treat the change separation in the transition state as a pair of point charges, $\pm ze$, separated by distance d, then, $\sigma = z^2d = 2{\cdot}45$ Å. The normal carbon–bromine bond distance being $r_1 = 2{\cdot}05$ Å, one can evaluate $(d - r_1)$ for different values of z:

z	0·8	0·9	0·95	1
d (Å)	3·84	3·03	2·73	2·45
$d - r_1$ (Å)	1·79	0·98	0·68	0·3

The distance $d - r_1$ is not, however, the bond elongation in the transition state because the positive charge is not localised on the methyl-carbon atom. The purpose of the above calculation is, however, to emphasise that even if the positive charge was localised on the methyl carbon one could still only obtain a rough value for the polarity of the activated complex. To proceed any further with such calculations either the charge or the amount of separation would have to be assumed, so that any consideration of the amount of covalent binding in the transition state is necessarily inconclusive.

(2) *Reaction of Diphenylmethyl Bromide with Chloride Ions.*—Chloride ions were supplied as tetraethylammonium chloride of normal isotopic abundance as well as labelled with ^{36}Cl. The radioactive salt was employed in order to overcome the uncertainty introduced by the hydrolysis of the alkyl halide when the saline material is extracted into water. The radioactive assay method proved to be particularly valuable in determining the extent of reaction in runs in the presence of high concentrations of saline bromide. The first-order coefficients of disappearance of diphenylmethyl bromide fall progressively within any given run. A set of initial first-order rate coefficients, k_i, is shown in Table 2 which illustrates that the initial first-order rate coefficients, $k_{i,obs}$, can be expressed with an accuracy of $\pm 3\%$ by the equation

$$k_i\,(\text{sec.}^{-1}) = k_1^{\mu} + (12 \times 10^{-5})[NEt_4Cl]$$

where k_1^{μ} is the first-order rate coefficient of the unimolecular component of displacement in a medium of ionic strength μ. Values for k_1^{μ} were independently obtained in a set of runs recorded in Table 2*b*. These are in good agreement with the corresponding values obtained in symmetrical exchange (Table 1*b*).

TABLE 2. *Initial first-order rate coefficients, k_i (sec.$^{-1}$), of displacement of bromine from diphenylmethyl bromide by chloride ions in nitromethane at 25·0°.*

(*a*)

10^2[Ph_2CHBr]	2·6	2·6	2·6	2·6	2·6	2·6
10^2[NEt_4Cl]	0·07	0·141	0·282	0·527	1·0	2·0 *
10^5k_i	1·75[R]	1·75[R]	1·78[P]	1·86[R]	1·95[P]	2·15[R]

R, Radioactive method, using $NEt_4{}^{36}Cl$; P, Potentiometric titrations.
* Run with 0·020M-Bu^n_4NCl gave $10^5k_i = 2{\cdot}12$.

(*b*)

10^2[Ph_2CHBr]	2·6	2·6	2·6	2·6	2·6
10^2[NEt_4Cl]	0·282	0·282	0·282	0·282	0·282
10^2[NEt_4ClO_4]	0·282	0·718	1·718	2·82 †‡	10·0
10^5k_i	1·79	1·83	1·90	1·95	2·56
μ	0·00564	0·010	0·020	0·031	0·103
$10^5k_1^{\mu}$	1·76	1·80	1·87	1·92	2·53

† Run with 0·0282M-$Bu^n_4NClO_4$ gave $10^5k_i = 1{\cdot}93$. ‡ Run with 0·0282M-NEt_4BF_4 gave $10^5k = 1{\cdot}98$.

(*c*)

10^2[Ph_2CHBr]	2·6	2·6	2·6	2·6
10^2[NEt_4Cl]	0·282	0·282	0·282	0·282
10^2[NEt_4Br]	0·282	0·527	2·82	10·0
10^5k_x	1·36	1·10	0·470	0·09
μ	0·00564	0·00809	0·03102	0·103
$10^5k_{1,\,calc}$	1·33 §	1·06 §	0·445 §	0·07 §

§ Where $10^5k_{1,\,calc} = 10^5k_1^{\mu}/(0{\cdot}35[Br^-]/[Cl^-] + 1)$ and $10^5k_2(NEt_4Cl) = 0{\cdot}0336$ sec.$^{-1}$.

The progressive fall of the forward rate within any given run is satisfactorily accounted for by the ionisation scheme

$$Ph_2CHBr \underset{k_{Br^-}}{\overset{k_1}{\rightleftharpoons}} Ph_2CH^+ + Br^- \xrightarrow{+\,Cl^-,\ k_{Cl^-}} Ph_2CHCl + Br^-$$

consideration being taken of the concurrent bimolecular reaction,

$$Ph_2CHBr + Cl^- \xrightarrow{k_2} Ph_2CHCl + Br^-$$

The presence of bromide ions reduces the unimolecular component of displacement by chloride ions so that

$$k_{obs} = \frac{k_1{}^u}{(k_{Br^-}[Br^-]/k_{Cl^-}[Cl^-]) + 1} + k_2[NEt_4Cl]$$

The progressive fall in k_{obs} in any given run is well represented by the above equation of $k_{Br^-}/k_{Cl^-} = 0{\cdot}35$. Added tetraethylammomium bromide depresses the initial rate of reaction (Table 2*a*) and here too a value of 0·35 for k_{Br^-}/k_{Cl^-} accounts satisfactorily for the observed depressions. This is illustrated at a low chloride ion concentration where $[NEt_4Cl] = 0{\cdot}0028$M, where the contribution of the bimolecular component is relatively small; $k_2\,[NEt_4Cl] = 0{\cdot}0336 \times 10^{-5}$ sec.$^{-1}$. It will be noticed that in the presence of sufficient saline bromide one can suppress the unimolecular component almost entirely, and that k_{Br^-}/k_{Cl^-} is throughout *ca.* 0·35. This indicates that the competitions between bromide and chloride ions take place at one and the same stage of ionisation.

(3) *Reaction of Diphenylmethyl Bromide with Azide Ions.*—The ions were introduced as tetraethylammonium azide and the progress of the reactions determined titrimetrically by following disappearance of azide ion, $-dN_3^-/dt$. The initial first-order rate coefficients of disappearance of diphenylmethyl bromide, $-d[Ph_2CHBr]/[Ph_2CHBr]dt = k_i$, calculated from such data, are given in Table 3. The initial first-order rate coefficients are satisfactorily expressed by the linear expression, $k_i = k_1 + k_2[NEt_4N_3]$, where at low ionic strength $10^5k_1 = 1{\cdot}75$ sec.$^{-1}$ and $10^5k_2 = 23{,}000$ sec.$^{-1}$ l. mole^{-1}. The magnitude of the bimolecular component of displacement by azide ions is so large that it proved impracticable to measure the intensity of the common-ion mass-law effect, $k_{Br^-}/k_{N_3^-}$. Rough measurements indicate that k_{Br^-}-$k_{N_3^-}$ is approximately $\frac{1}{5}$.

TABLE 3. *Initial first-order rate coefficients, k_i (sec.$^{-1}$), of displacement of bromine from diphenylmethyl bromide by azide ions in nitromethane at 25·0°.*

$10^3[Ph_2CHBr]$	0·191	0·191	1·91	1·91	1·91	1·91
$10^3[NEt_4N_3]$	0·0045	0·009	0·150	0·24	0·49	0·67
10^5k_i	2·78	3·8	36	57	112	159

Discussion.—(*a*) In nitromethane, the first-order component of substitution of diphenylmethyl bromide by chloride, radiobromide, and azide ions is practically the same: $k_1 = 1{\cdot}75 \times 10^{-5}$ sec.$^{-1}$. On the other hand, the second-order component for substitution by azide ions is 128 times larger than that for bromide ions and 1900 times larger than that for chloride ions, while the relative capacity for capturing Ph_2CH^+ is: N_3^- [*ca.* 5) > Cl^- (2·86) > Br^- (1·0). (*b*) Added perchlorate ions increase the first-order component of substitution but decrease the second-order component. (*c*) Common ions decrease the first-order component of non-symmetric substitution, and can suppress practically the entire first-order component. The intervention coefficient is the same up to *ca.* 90% repression of rate.

Results (*a*), (*b*), and (*c*) suggest that the first- and second-order components represent a uni- and a bi-molecular substitution respectively. The unimolecular substitution seems to proceed through free carbonium ions.

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Experimental

Materials.—Nitromethane was dried, fractionated, and chromatographed as previously described.[2] Diphenylmethyl bromide was prepared (*a*) by the bromination of diphenylmethane and (*b*) from diphenylmethanol and phosphorus tribromide. The products from (*a*) and (*b*) were practically identical after distillation, having b. p. 140—145°/3 mm. Tetraethylammonium salts were prepared as before.[8]

Kinetic Measurements.—Temperature control was ±0·01° at 25·0°. Reaction mixtures (50 c.c.) were prepared by the addition of the necessary amount of previously prepared standard solutions of reagents and solvent, both preheated to 25·0°, to a weighed sample of diphenylmethyl bromide. In reactions with tetraethylammonium azide, aliquot portions were delivered into dry acetone at −80° and titrated with standard acid, lacmoid being used as indicator (in acetone azide ions behave as a strong base towards lacmoid).

Radioactive Runs.—(*a*) Known volumes of the reaction mixture containing diphenylmethyl bromide and tetraethylammonium radiobromide, with or without saline perchlorate, were withdrawn and run into 100 c.c. of cold dry ether. The precipitated salt was washed with fresh ether and dissolved in 15 c.c. of water, and its radioactivity measured with a liquid Geiger counter and standard scaling equipment. Each sample was counted twice. From the decay curves, which corresponded within experimental error with those expected for ^{82}Br, values were read to give counts for each sample at the same but otherwise arbitrary time. The bromide content of each sample was also determined and thus the activities as measured were corrected to give specific activities, referring in each experiment to the same arbitrary concentration of bromide ion. First-order rate coefficients, k_{obs} (sec.$^{-1}$), were deduced from the formula:[9]

$$k_{obs} = \frac{2{\cdot}303b}{(a+b)t} \log \left\{ 1 - \frac{x_0}{c}\left(1 + \frac{b}{a}\right) \right\} \Big/ \left\{ 1 - \frac{x}{c}\left(1 + \frac{b}{a}\right) \right\}$$

where t is the time in sec., a and b the concentrations of diphenylmethyl bromide and tetraethylammonium bromide respectively, $c - x_0$ and $c - x$ the specific activities at kinetic zero and time t respectively, and c is the specific activity of the initial reaction mixture. A convenient way to use this formula is to plot $\log \{1 - (a + b)x/aC\}$ against t and multiply the slope of the line by $-2{\cdot}303b/(a + b)$.

(*b*) Radiochloride, ^{36}Cl, is a long-lived isotope and requires no correction for decay. The reaction with diphenylmethyl bromide is a non-symmetric exchange and a loss in the radioactivity of the saline precipitate is a direct consequence of a decrease in the chloride-ion concentration. Aliquot portions were run into 100 c.c. of dry cold ether, and the precipitate was washed with ether, dissolved in water, and counted as in (*a*). If C_0 and C_t are the initial count and the count at time t respectively, then $[Cl^-]_t = [Cl^-]_0 C_t/C_0$ and

$$k_{obs} = \frac{2{\cdot}303}{t} \log \frac{[[Ph_2CHBr]_0}{[Ph_2CHBr]_0 - \{[Cl]_0 - [Cl]_t\}}$$

Isolation of Products.—Diphenylmethyl azide was isolated in 96% yield from the reaction with tetraethylammonium azide. Diphenylmethyl chloride was isolated in 95% yield from the reaction with *excess* of tetraethylammonium chloride.

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[8] Pocker, *J.*, 1959, 2319.
[9] Hughes, Ingold, Mok, Patai, and Pocker, *J.*, 1957, 1220.

793. *Intermediates in Aralkyl Systems. Part III.*[1] *Kinetics and Mechanisms of Substitution of Diphenylmethyl Bromide by Amines in Nitromethane.*

By Y. Pocker.

The reactions of diphenylmethyl bromide with triethylamine, pyridine, aniline, and *NN*-dimethylaniline have been studied kinetically in nitromethane. Analysis of the products indicated *N*-substitution with the first three amines but *C*-substitution in the ring with *NN*-dimethylaniline. With the first three amines the upper limit to the amount of depression by common ions was found to be the entire first-order component while the second-order component was unaffected except for a general positive salt effect. With *NN*-dimethylaniline, however, there was no limit to the amount of depression by bromide ion. It is suggested that the first- and the second-order component represent S_N1 and S_N2 mechanisms respectively, and that notwithstanding the high rates of racemisation of some aralphyl halides in nitromethane, in the S_N1 component of the present system chemical capture takes place at the free carbonium ion stage. The second-order component in *NN*-dimethylaniline appears to be a bimolecular substitution at nitrogen followed by an easy rearrangement to the *C*-substituted derivative. This rearrangement proceeds through a capturable intermediate.

It is of interest to examine whether the upper limit to the amount of depression by a common ion can be used to confirm the presence of two concurrent and independent mechanisms of substitution, Thus when the S_N1 component of substitution proceeds *via* kinetically free ions, the upper limit to the amount of depression should be the entire first-order component, leaving the second-order component practically unaffected except for a general salt effect. An attempt was therefore made first to establish whether heterolysed but undissociated intermediates have to be postulated to explain the kinetics of reaction of diphenylmethyl bromide with neutral nucleophiles in nitromethane, and, secondly, to test the validity of the criterion suggested above for concurrent mechanisms in substitution reactions with non-saline nucleophiles. A detailed investigation of the reactions of diphenylmethyl bromide with various amines has now been carried out.

(1) *Reaction of Diphenylmethyl Bromide with Triethylamine.*—This reaction does not follow the simple first-order rate law. First-order rate coefficients, k_x, of disappearance of diphenylmethyl bromide, fall progressively. A set of initial first-order rate coefficients, k_i, is shown in Table 1*a* which illustrates that the first-order rate coefficients in diphenylmethyl bromide do not depend upon its concentration. The dependence on triethylamine is well represented by the equation

$$k_i = 1{\cdot}75 \times 10^{-5} + 16{\cdot}5 \times 10^{-5}[NEt_3]$$

where k_i is in sec.$^{-1}$ (Table 1*a*).

When, however, the triethylamine concentration is lower than about one-twentieth of that of diphenylmethyl bromide, truly initial first-order rate coefficients cannot be directly determined from the experimental readings because of the mass-law depression. Common-ion retardation was independently established by observing the effect of added tetraethylammonium bromide on the initial rates of the forward reaction. If the process which is of first order in diphenylmethyl bromide and of zeroth order in triethylamine is represented by

$$Ph_2CHBr \underset{k_{Br^-}}{\overset{k_1}{\rightleftharpoons}} Ph_2\overset{+}{C}H + Br^- \xrightarrow{+NEt_3,\ k_{NEt_3}} Ph_2CH\overset{+}{N}Et_3 + Br^-$$

[1] Part II, Pocker, preceding paper.

and the process which is of first order in both alkyl halide and amine is represented by

$$NEt_3 + Ph_2CHBr \xrightarrow[S_N2]{k_s} [Et_3N^{\delta+}\ldots CHPh_2\ldots Br^{\delta-}] \longrightarrow Ph_2CH\overset{+}{N}Et_3 + Br^-$$

then

$$k_x = \frac{k_1}{(k_{Br^-}[Br^-]_x/k_{NEt_3}[NEt_3]_x) + 1} + k_2[NEt_3]_x$$

Indeed, a plot of $k_1/k_x - k_2[NEt_3]_x)$ against $[Br^-]_x/[NEt_3]_x$ has the slope $k_{Br^-}/k_{NEt_3} = 1{\cdot}5$ and, as would be expected from the above equation, intercept of $+1{\cdot}0$. In the absence of added saline bromide, the progressive fall in the rate of forward reaction in any given run

TABLE 1. *Initial first-order rate coefficients, k_1 (sec.$^{-1}$), of reaction between triethylamine and diphenylmethyl bromide in nitromethane at 25·0°.*

(*a*)

$10^3[Ph_2CHBr]$	2·0	2·0	2·0	2·0	2·0	2·0	10	10	10	10	10
$10^3[NEt_3]$	0·20	0·50	1·0	2·0	3·0	4·0	1·0	2·0	3·0	4·0	5·0
10^5k_1	1·7	1·80	1·91	2·08	2·25	2·42	1·9	2·08	2·22	2·45	2·58

(*b*) $[Ph_2CHBr] = 0{\cdot}020$M.

$10^3[NEt_3]_1$	0·1	0·2	0·25	0·5	0·75	1
$10^4[NEt_3]_x$	0·47	1·04	1·5	3·5	5·8	8·3
$([Br^-]/[NEt_3])_x$	1·13	0·924	0·667	0·429	0·293	0·205
10^5k_x	0·65	0·74	0·91	1·07	1·16	1·34
$10^5k_{1,\ calc.}$	1·75	1·74	1·82	1·77	1·67	1·75

* $k_{1,\ calc.} = k_x\{1{\cdot}5([Br^-]/[NEt_3]_x) + 1\}$

(*c*) $[Ph_2CHBr] = 0{\cdot}020$M; $[NEt_3] = 0{\cdot}0050$M.

$10^2[NEt_4ClO_4]$	1·0	2·0	3·0	4·0	6·0
10^5k_1	1·87	1·97	2·02	2·14	2·32

(*d*) $[Ph_2CHBr] = 0{\cdot}020$M, $[NEt_3] = 0{\cdot}0050$M.

$10^2[NEt_4Br]$	0·125	0·25	0·50	0·75	1·0
10^5k_1 †	1·3	1·0	0·77	0·61	0·52

† $k_1{}^{\mu}/(k_1 - k_2[NEt_3])$ is plotted against $[NEt_4Br]/[NEt_3]$ in Fig. 1.

(at low ionic strength) is fairly well represented by $10^5k_1 = 1{\cdot}75$ sec.$^{-1}$ and $k_{Br^-}/k_{NEt_3} = 1{\cdot}5$ at 25·0°. This means that diphenylmethyltriethylammonium bromide and triethylamine hydrobromide, which are the two saline products in this reaction, have in nitromethane about the same capacity to capture the reaction intermediate as has tetraethylammonium bromide. The mass-law effect also accounts for the low first-order rate coefficients obtained when $[NEt_3]/[Ph_2CHBr] < \frac{1}{20}$. This effect arises because in those instances the balance of competition of the two consumers of formed carbonium ions is not what it should be when truly initial rates are determined, *i.e.*, $k_{Br^-}[Br^-] > k_{NEt_3}[NEt_3]$, leading to an increase in k_x with $[NEt_3]$, similar to that encountered in S_N2C^+ behaviour.[2] As an extreme example let us take $[NEt_3]/[Ph_2CHBr] = 0{\cdot}01$. The first kinetically significant sample withdrawn from the reaction mixture corresponded to *ca.* 0·5% of reaction with respect to diphenylmethyl bromide which is, however, *ca.* 50% of reaction with respect to this low concentration of triethylamine. The ratio $[Br^-]/[NEt_3]$ for this point is *ca.* 1, and since $k_{Br^-}/k_{NEt_3} = 1{\cdot}5$, one obtains $k_x \sim 0{\cdot}4\ k_1$. Table 1*b* illustrates and analyses similar examples.

When $[NEt_3] = 0{\cdot}005$M the contribution of the second-order component is low and the variation in k_1 with added tetraethylammonium perchlorate can be analysed as being mainly due to variations in k_1. Indeed, the ionic-strength effects on k_1 are similar (Table 1*c*) to those already encountered in symmetrical exchange studies (preceding paper).

(2) *Reaction of Diphenylmethyl Bromide with Aniline.*—The stoicheiometry of this reaction is $Ph_2CHBr + 2PhNH_2 \longrightarrow Ph_2CH{\cdot}NHPh + PhNH_3^+\}Br^-$. A set of initial first-order rate coefficients is shown in Table 2 which illustrates that the first-order rate coefficients in diphenylmethyl bromide do not depend upon its concentration.

[2] Gelles, Hughes, and Ingold, *J.*, 1954, 2924.

TABLE 2. *Initial first-order rate coefficients, k_1 (sec.$^{-1}$), of reaction of diphenylmethyl bromide and aniline in nitromethane at 25·0°; effects of added tetraethylammonium bromide and perchlorate.*

(*a*) 10^2[Ph_2CHBr] ...	0·25	0·5	1·0	2·0	3·0	5·0	0·25	0·25	0·25	0·25
10^2[$PhNH_2$]	0·5	0·5	0·5	0·5	0·5	0·5	0·125	0·25	0·5	1·0
10^5k_1	2·3	2·35	2·32	2·3	2·2	2·1	1·86	2·04	2·30	2·9
10^2[Ph_2CHBr] ...	2·0	2·0	2·0	2·0	2·0	2·0	2·0			
10^2[$PhNH_2$]	0·5	1·0	2·0	3·0	4·0	5·0	10			
10^5k_1	2·3	2·86	3·95	5·05	6·15	7·25	12·7			

(*b*) [Ph_2CHBr] = 0·02M; [$PhNH_2$] = 0·005M.									
10^2[NEt_4ClO_4] ...	1·0	2·0	4·0	6·0	20·0	10^2[NEt_4Br] ...	0·50	1·0	2·0
10^5k_1	2·35	2·45	2·7	2·9	3·2	10^5k_1	1·65	1·37	1·1
						k_{Br^-}/k_{PhNH_2} ...	0·61	0·60	0·61

(*c*) [Ph_2CHBr] = 0·020M; [NEt_4ClO_4] = 0·20M.

10^2[$PhNH_2$]	0·5	1·0	2·0
10^5k_1	3·2	3·8	5·1

[Ph_2CHBr] = 0·020M; [NEt_4Br] = 0·20M.

10^2[$PhNH_2$]	0·2	0·5	0·75	1·0	1·5	2·0
10^5k_1	0·23	0·57	0·86	1·2	1·9	2·4

The dependence on aniline concentration is well expressed by the equation $k_1 = k_1^{\mu} + k_2^{\mu}[PhNH_2]$. At low ionic strength $10^5k_1^{\mu} = 10^5k_1 = 1{\cdot}75$ sec.$^{-1}$ and $k_2^{\mu} = k_2 = 110 \times 10^{-5}$ sec.$^{-1}$ l. mole^{-1}. The addition of tetraethylammonium bromide depresses the initial rate of the forward reaction. The depression is well represented by the equation. The depression is well represented by the equation

FIG. 1. *Reaction of diphenylmethyl bromide with triethylamine in the presence of added tetraethylammonium bromide in nitromethane solution at 25·0°.*

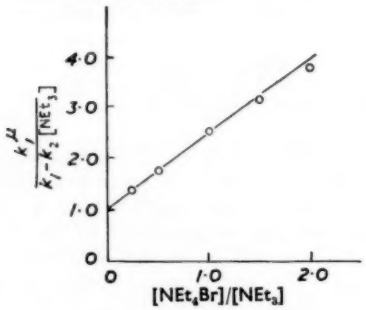
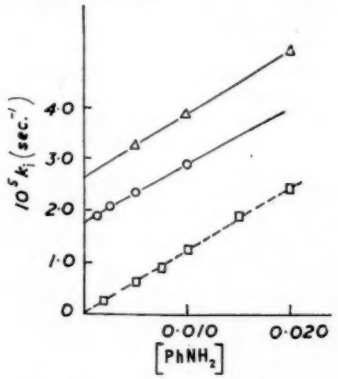


FIG. 2. *Reaction of diphenylmethyl bromide with aniline ○; in the presence of 0·20M-NEt_4ClO_4 △; and in the presence of 0·20M-NEt_4Br □.*



$$k = \frac{k_1}{(k_{Br^-}[Br^-]/k_{PhNH_2}[PhNH_2]) + 1} + k_2[PhNH_2]$$

where at 25·0° at low ionic strength $k_{Br^-}/k_{PhNH_2} = 0{\cdot}61$. With [$NEt_4Br$] = 0·20M the first-order component is almost entirely suppressed so long as [NEt_4Br]/[$PhNH_2$] $\geqslant 10$ and the forward reaction is almost entirely a second-order process which can be identified with the S_N2 component at an ionic strength of 0·2M-NEt_4ClO_4. Indeed, a plot of the maximally supressed rate against the concentration of aniline passes through the origin and the line is parallel to that of the unsuppressed rate at the same ionic strength (Fig. 2).

(3) *Reaction of Diphenylmethyl Bromide with Pyridine.*—This reaction was followed by the disappearance of amine during the reaction $Ph_2CHBr + C_5H_5N \longrightarrow Ph_2CH\overset{+}{N}C_5H_5\}Br^-$ Acetone–glacial acetic acid (4 : 1,v/v) was a suitable quenching medium. The acetic acid does not solidify from it even at −80°, diphenylmethyl bromide is inert in it at low

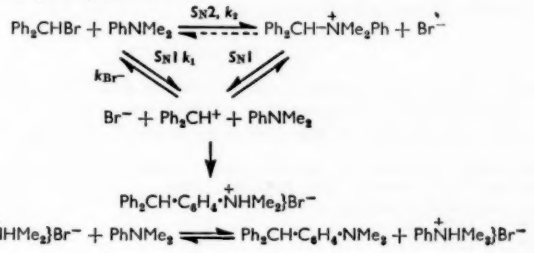
temperatures, and pyridine is quantitatively converted into acetate ions which can be satisfactorily titrated with standard perchloric acid in glacial acetic with Bromothymol Blue as indicator. A set of initial first-order rate coefficients, k_i (sec.$^{-1}$), is shown in Table 3. The dependence of k_i on pyridine concentration is satisfactorily expressed by $10^5k_i = 1{\cdot}75 + 65[C_5H_5N]$. From the depression of the initial rate by added tetraethylammonium bromide one calculates, at low ionic strength, $k_{Br^-}/k_{C_5H_5N} = 3{\cdot}4$ at 25·0°. With $[NEt_4Br] = 0{\cdot}2$M the first-order component k_1, is almost entirely suppressed at all pyridine concentrations below 0·05M and the forward reaction in this region is a second-order process: $10^5k_i = 75[C_5H_5N]$.

TABLE 3. *Initial first-order rate coefficients, k_i (sec.$^{-1}$), of reaction of diphenylmethyl bromide with pyridine in nitromethane at* 25·0°. $[Ph_2CHBr] = 0{\cdot}0097$M.

(*a*) $10^2[C_5H_5N]$	0·142	0·284	0·568	1·14	2·28	
10^5k_i	1·82	1·95	2·03	2·40	3·27	
(*b*) $10^2[C_5H_5N]$	1·14	1·14	1·14			
$10^2[NEt_4Br]$	0·237	0·593	1·18			
10^5k_i	1·76	1·36	1·14			
$k_{Br^-}/k_{C_5H_5N}$ *	3·4	3·5	3·3			
(*c*) $[NEt_4Br] = 0{\cdot}20$M						
$10^2[Ph_2CHBr]$	0·97	0·97	0·97	1·94	1·94	3·88
$10^2[C_5H_5N]$	0·50	1·0	2·0	3·0	4·0	5·0
10^5k_i	0·38	0·75	1·45	2·3	3·1	3·8

* $(k_{Br^-}/k_{C_5H_5N})([Br^-]/[C_5H_5N]) = k_1{}^{\mu}/(k_i - k_2[C_5H_5N]) - 1$

(4) *Reaction of Diphenylmethyl Bromide with* NN-*Dimethylaniline.*—This reaction was followed by the disappearance of amine during the reaction (see previous section). The first-order rate coefficients of disappearance of diphenylmethyl bromide did not show any appreciable progressive fall within any given run and it was therefore suspected that a weak electrolyte is being produced, *i.e.*, the hydrobromide of a weak tertiary amine rather than a quaternary ammonium bromide. Since the hydrobromide of a weak amine behaves on titration as an acid in acetone with respect to lacmoid the rates of " acid " production were similarly investigated (Table 4*a*). The results obtained illustrate that $-d[Amine]/dt = +dH^+/dt$ so that a *C*-substitution rather than an *N*-substitution must take place: $Ph_2CHBr + 2PhNMe_2 \longrightarrow Ph_2CH{\cdot}C_6H_4{\cdot}NMe_2 + PhN^+Me_2H\ Br^-$. This conclusion was confirmed by product analysis, the *para*-substituted diphenylmethyl derivative of *NN*-dimethylaniline being recovered in 94% yield. The dependence of the initial first-order rate coefficients of disappearance of diphenylmethyl bromide k_i (sec.$^{-1}$) on *NN*-dimethylaniline is well represented by the equation $10^5k_i = 1{\cdot}75 + 135[PhNMe_2]$. While a substitution in the *NN*-dimethylaniline ring by the electrophilic carbonium ion produced in the unimolecular component is easily visualised, the problem arises how can ring substitution proceed *via* an S_N2 transition state with respect to diphenylmethyl bromide. The products were therefore analysed at a concentration where the second-order component was 10 times larger than the first-order component and again the product was >90% *p*-diphenylmethyl-*NN*-dimethylaniline. Conceivably, the second-order component represents an S_N2 attack on nitrogen followed by an easy unimolecular rearrangement of the diphenylmethyl group to the *para*-position.



If this rearrangement proceeds *via* a carbonium ion then both the first- and the second-order component should be depressed by added tetraethylammonium bromide. Indeed, this is the only reaction where tetraethylammonium bromide was found to suppress both the first- and the second-order component of substitution (Table 4*b*).

TABLE 4. *First-order rate-coefficients, k_A or k_{H^+} (sec.$^{-1}$). of reaction of diphenylmethyl bromide and* NN*-dimethylaniline in nitromethane at* 25·0°.

(*a*)	10^3[Ph_2CHBr]	0·13	1·3	1·3	1·3	1·3	1·3
	10^3[PhNMe] ...	0·15	0·15	0·45	1·13	2·26	3·39
	10^5k_A	1·95	1·93	2·35	3·25	4·70	—
	$10^5k_{H^+}$	1·95	1·90	2·37	3·22	4·78	6·25

(*b*)	10^3[Ph_2CHBr]	1·3	1·3	1·3	1·3
	10^3[$PhNMe_2$]...	1·13	2·26	1·13	4·51
	10^3[NEt_4Br] ...	2·37	2·26	5·98	0·598
	10^5k_A	1·60	1·01	0·865	0·47

k_A was calculated from $-$d[Amine]/dt and k_{H^+} from $+$d[R_3NH^+]/dt.

Discussion.—(*a*) While the stereochemical behaviour of some aralkyl halides in nitromethane indicates that in the absence of electrophilic catalysis racemisation takes place before dissociation,[3] common-ion repression experiments indicate the absence of a chemically capturable intermediate in the diphenylmethyl system before the free carbonium ion stage.

(*b*) Compelling evidence for the operation of two concurrent processes, S_N1 and S_N2, comes from observations on the rates of reactions maximally depressed by common ions.

(*c*) The capturing capacity of the various reagents employed towards the diphenylcarbonium ion, $PhNH_2$ (1·7) > Br^- (1·0) > NEt_3 (0·67) > C_5H_5N (0·29) > $PhNMe_2$, does not follow their nucleophilic power towards diphenylmethyl bromide, Br^- > $PhNMe_2$ > $PhNH_2$ > C_5H_5N > NEt_3, as measured by the ratios of the second-order components.

(*d*) The particularly low reactivity of NEt_3 in the S_N2 process may be due to steric hindrance.

(*e*) On a free-energy basis, the reactions where the carbonium ion reacts faster with the common ion than with amine are not strictly S_N1. They become, however, S_N1 in the limit, *i.e.*, when the concentration of reagent Y is sufficiently high that $k_Y[Y] > k_{Br^-}[Br^-]$, leading to $k_x \longrightarrow k_1$. With 2,6-lutidine the first-order rate coefficient as determined in the initial stages of reaction rises steadily and approaches the values of k_1 only at relatively high amine concentrations, but with more sterically hindered amines one observes a transition to S_N2C^+ behaviour.[4]

(*f*) The kinetics of the unimolecular component with amines embody three features: (i) the initial rates of the various substitutions are the same, (ii) the ionic strength effects are similar and positive, and (iii) common ions can depress the entire unimolecular component.

(*g*) The kinetics of the bimolecular component of substitution by amines show a positive ionic-strength effect as would accord with a reaction whose transition state is more polar than its initial state. This result should be contrasted with the negative ionic-strength effect observed in the bimolecular component of substitution by anions (preceding paper).

(*h*) The criterion used to distinguish concurrent from borderline mechanisms is limited to cases where the common-ion repression can successfully compete with the sum of forward reactions (substitutions and eliminations.)

EXPERIMENTAL

Materials.—These were prepared and purified as described previously.[5,6]

Kinetic Measurements.—Temperature control was ±0·01° at 25·0°. Reaction mixtures were prepared as indicated in the preceding paper.[1] To the reaction with triethylamine,

[3] Pocker, paper presented at the Informal Faraday Society meeting, Leeds, September, 1958. For abstract, see *Trans. Faraday Soc.*, 1959, **55**, 1266.
[4] Pocker, unpublished results.
[5] Pocker, *J.*, 1958, 240.
[6] Pocker, *J.*, 1959, 1179.

aliquot portions were delivered into dry acetone at −80° and titrated with standard acid with lacmoid indicator. To reactions with the weaker tertiary amines, pyridine and *NN*-dimethylaniline, aliquot portions were quenched in acetone–acetic acid (4 : 1, v/v) at −80° and titrated with standard perchloric acid dissolved in glacial acetic acid with Bromothymol Blue as indicator. In reactions where the product was the hydrobromide of a weak amine, *e.g.*, anilinium and *NN*-dimethylanilinium hydrobromide, aliquot portions were quenched in acetone at −80° and titrated with standard alkali with lacmoid indicator. An illustrative run is in Table 5.

TABLE 5. *Illustrative run.* $[Ph_2CHBr]_i = 0{\cdot}020$M. $[NEt_3]_i = 0{\cdot}010$M.

Time (sec.)	0	130	265	426	536	830	1020
$10^3(a - x)$	20·0	19·95	19·9	19·84	19·8	19·7	19·64
10^5k_x (sec.$^{-1}$)	—	1·91	1·90	1·88	1·87	1·83	1·83
Time (sec.)	1400	1760	2160	2400	3100	5400	
10^3 $(a - x)$	19·5	19·38	19·26	19·2	19·0	18·4	
10^5k_x (sec.$^{-1}$)	1·81	1·78	1·74	1·70	1·66	1·54	

The value of k_x when $[Br^-]/[NEt_3] = 0$ is $k_1 = 1{\cdot}91 \times 10^{-5}$ sec.$^{-1} = k_1 + k_2[NEt_3] = 1{\cdot}75 \times 10^{-5} + 16 \times 10^{-5}$ [0·01].

The various values of k_x are well represented by the general equation given on p. 3945, if $k_{Br^-}/k_{NEt_3} = 1{\cdot}5$.

Isolation of Products.—Diphenylmethyltriethylammonium bromide, isolated in 88% yield * from the reaction with triethylamine, had m. p. 166° (decomp.) (Found: Br^-, 22·8. Calc. for $C_{19}H_{26}NBr$: Br^-, 22·9%). 4-Dimethylaminotriphenylmethane, isolated in 94% yield from the reaction with dimethylaniline, had m. p. 131° (Found: C, 88·0; H, 7·6; N, 4·9. Calc. for $C_{21}H_{21}N$: C, 87·8; H, 7·4; N, 4·8%). It is a weak base towards lacmoid in acetone, but liberates acetate ions in acetone–glacial acetic acid (4 : 1, v/v) which when neutralised indicate equiv. of 284. (Calc.: *M*, 287). The compound was independently synthesised (*a*) by the condensation of diphenylmethanol with *NN*-dimethylaniline in the presence of phosphoric oxide at 180°,[7a] and (*b*) from 4-dimethylaminobenzaldehyde and phenylmagnesium bromide.[7b] Recrystallised from chloroform, it had m. p. 133°, alone or mixed with a reaction sample (lit.,[7] m. p. 133°). *N*-Diphenylmethylpyridinium bromide, m. p. 204° (decomp.), was obtained in 85% yield (Found: Br^-, 24·4. Calc. for $C_{18}H_{16}NBr$: Br^-, 24·6%).

The author thanks Professor E. D. Hughes, F.R.S., and Sir Christopher Ingold, F.R.S., for their interest, and Messrs. D. W. Hills and A. B. Spiers for technical assistance.

* This refers to conditions where $[NEt_3] > [Ph_2CHBr]$. However, when $[Ph_2CHBr] > [NEt_3]$ some triethylamine hydrobromide was also isolated. It may be that this product arises when the ratio $[Br^-]/[NEt_3]$ becomes so large that substitution by NEt_3 is reduced to a point where reaction with $CH_2NO_2^-$ (formed in the reaction $CH_3NO_2 + NEt_3 \rightleftharpoons CH_2NO_2^-\}NEt_3H^+$) is no longer negligible.

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[7] (*a*) Fischer, *Annalen*, 1880, **206**, 113; (*b*) Sachs and Sachs, *Ber.*, 1905, **38**, 523.

794. *Diphosphine Dioxides. Part I. Some Representative Diphosphine Dioxides with a Tetra-, Penta-, and Hexa-methylene Bridge.*

By Gennady M. Kosolapoff and Robert F. Struck.

Ten members of the novel class of organophosphorus compound $[R_2P(O)]_2[CH_2]_x$, where $x = 4$, 5, or 6, have been synthesized from di-Grignard reagents. The preparation of dialkylphosphinic acids has been improved.

In our synthetic studies of organophosphorus compounds it appeared advisable to examine the possible series of organic diphosphine dioxides, *i.e.*, compounds of the general class, $[R_2P(O)]_2[CH_2]_x$, with a variety of radicals R and various values of x. These compounds are the closest phosphorus-bearing analogues of diketones and it was obviously interesting to examine the variation of the properties of such compounds with changes in the structural factors R and x.

The present paper deals with the synthesis of several compounds of this class with x values of 4, 5, and 6.

Probably the most satisfactory route to these substances appeared to be the reaction of di-Grignard reagents with appropriate phosphinyl chlorides:

$$2R_2P(O)Cl + [CH_2]_x(MgX_2)_2 \longrightarrow [R_2P(O)]_2[CH_2]_x + 2MgXCl$$

This route is suitable for the preparation of these substances with values of $x = 4$ and higher. It was felt that the separation of the two PO groups by more than six methylene bridge units probably would not produce any further interesting changes in the properties of these compounds.

Accordingly nine substances were prepared in this category with R = methyl, n-butyl, or phenyl; one compound with R = ethyl was also synthesized for reasons which appear below.

The syntheses proceeded satisfactorily but it was noted that the conventional aqueous treatment of the reaction mixtures resulted in the precipitation of the desired compounds in the form of complexes or addition compounds with the magnesium halides. This had not been reported in the analogous Grignard syntheses of the simple tertiary phosphine oxides. After the removal of the inorganic addend in the usual manner, the compounds with R = ethyl, n-butyl, and phenyl were readily purified and isolated as solvent-free substances. The dioxides with R = methyl, however, retained crystallization solvents or moisture most tenaciously. These solvent-bearing products possessed rather sharp melting points and were convertible into the solvent-free form only by rather drastic heating *in vacuo*. The solvent-retention progressed quite evidently with decrease in the size of the methylene bridge. The methyl members of the group also proved to be resistant to the nitric acid–permanganate method of oxidative decomposition for phosphorus analysis, a method which was satisfactory for the other members of the group, including the ethyl derivative, which was prepared at this juncture in order to verify the unusual resistance of the methyl members specifically.

The synthetic route used by us required the preparation of phosphinic acids. Some minor improvements were introduced into the previously described procedure.

Experimental

Synthesis of Phosphinic Acids and Phosphinyl Chlorides.—The previously reported [1] Grignard synthesis of phosphinic acids was changed as indicated below. A Grignard reagent, prepared from 3·0 moles of bromobenzene and 3·0 g.-atoms of magnesium in 1 l. of absolute ethyl ether, was treated during 6 hr. with 135 g. (slightly under one mole) of diethyl hydrogen

[1] Kosolapoff and Watson, *Amer. Chem. J.*, 1951, **73**, 4101, 5466.

phosphonate with good stirring, then the mixture was refluxed overnight. The product was dropped into ice-water and the mixture was acidified with *ca.* 170 ml. of concentrated hydrochloric acid. The ether evaporated in the course of this operation and its residues were removed by gentle warming. Bromine was added dropwise with stirring until a faint permanent color remained. The precipitated diphenylphosphinic acid was collected, dissolved in aqueous potassium hydroxide, and reprecipitated by acidification. After drying by means of benzene–water azeotropic distillation, there were obtained 161 g. (75%) of diphenylphosphinic acid, m. p. 194—195°. A 78% yield was obtained when the bromine was added to a dioxan solution of the oily layer which had separated after the acidification of the original reaction miture. If a small amount of an alkali-insoluble material is obtained after the oxidation with bromine, as described above, this material (evidently diphenylphosphine oxide) may be readily oxidized to the desired acid by treatment with a small volume of potassium permanganate solution.

The diphenylphosphinic acid, in dry benzene, was treated with an equimolar amount of phosphorus pentachloride at the b. p. with stirring overnight. Distillation gave consistent 88% yields of diphenylphosphinyl chloride, b. p. 227—230°/10 mm.

Di-n-butylphosphinic Acid and Its Chloride.—The acid was prepared in 78—87% yields by the technique described above. Treatment of this with phosphorus pentachloride gave up to 92% of the corresponding chloride, b. p. 163—166°/22 mm.

Diethylphosphinic Acid and Its Chloride.—While the synthesis of the acid was as described above, its isolation had to be performed differently, owing to the solubility of the acid in aqueous media. The original reaction mixture solidified after addition of the phosphonate, and the whole was refluxed overnight without stirring. After the aqueous treatment and addition of bromine, the entire mixture was evaporated under water-pump vacuum at 50° in a rotating glass evaporator. The residue was treated with a solution of 330 g. of potassium hydroxide in aqueous ethanol, the resulting precipitate of magnesium hydroxide was filtered off, and the filtrate was strongly acidified with hydrochloric acid and evaporated to dryness under water-pump vacuum. The residue was triturated with ethanol, and the alcoholic extract was evaporated to dryness and treated with an aqueous slurry of lead oxide until the mixture became slightly basic. The solids were filtered off and the filtrate was freed from lead by treatment with hydrogen sulphide. The viscous residue, after the evaporation of the solvent, was distilled *in vacuo*, yielding diethylphosphinic acid (22%), b. p. 194—195°/21 mm. This was converted into the chloride, as described above, the yield being 86% of a product, b. p. 134—135°/52 mm.

The working time required for this procedure is considerably less than for the previous procedure which employed thiophosphoryl chloride and a Grignard reagent.

The bromination–oxidation technique used in these preparations is more convenient than the previously used hydrogen peroxide oxidation, especially for relatively large runs which become hazardous under the other procedure.

Dimethylphosphinic Acid and Its Chloride.—These were prepared as described recently by Reinhardt *et al.*[2] We found that while a substantially quantitative yield of the acid is obtained if the mixture is stirred overnight (Reinhardt and his co-workers failed to specify the duration of the reaction), the yield fell to *ca.* 50% if the reaction is run at the b. p. for only 6 hr. A similar yield (*ca.* 50%) resulted when the reactants were kept for 15 days at room temperature. The acid was converted in nearly quantitative yield into the chloride, b. p. 202—206°.

The Diphosphine Dioxides.—In a typical preparation, diphenylphosphinic chloride (22·0 g.) in dry ether (50 ml.) was added dropwise to the Grignard reagent prepared from tetramethylene bromide (12·1 g.) and magnesium (2·7 g.) in ether (100 ml.). The mixture was refluxed with stirring for 20 hr., then poured on ice (50 g.), and the precipitated complex of the diphosphine dioxide and magnesium halide was treated *in situ* with a solution of potassium hydroxide (20 g.) in ethanol (200 ml.). Magnesium hydroxide was filtered off and the filtrate adjusted to pH 6 with hydrochloric acid, filtered again, and evaporated to dryness *in vacuo*. The residue was rubbed with 10% aqueous potassium hydroxide (50 ml.) to remove any diphenylphosphinic acid. The oily layer was separated and the aqueous layer was extracted with benzene (50 ml.) to recover a small amount of emulsified product. The combined organic material was evaporated *in vacuo* and the residue was chilled overnight in a refrigerator, yielding 19·3 g. (94%) of the crude product. After recrystallization from dry benzene (100 ml.), this gave the first crop of 7·5 g. (39%) of pure $[Ph_2P(O)]_2[CH_2]_4$. Alternatively, the crude product may be

[2] Reinhardt, Bianchi, and Möller, *Chem. Ber.*, 1957, **90**, 1658.

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vacuum-distilled, boiling without decomposition at 290—291°/1·6 mm. and melting at ~110°. After recrystallization from dry benzene, *tetramethylenebis(diphenylphosphine oxide)* melted at 154—155° (Found: P, 13·2, 13·3. $C_{28}H_{28}O_2P_2$ requires P, 13·5%).

The remaining *diphosphine dioxides* (see Table) were prepared similarly. The synthesis of the methyl members required the addition of the dimethylphosphinic chloride in benzene solution owing to the low solubility of this chloride in ether.

					P, %		C, %		H, %	
R	*x*	B. p./mm.	M. p.	Yield	found	calc.	found	calc.	found	calc.
Ph	5	326—327°/0·27	119—120°	55%	13·00	13·12				
Ph	6	292—294°/0·20	196—198°	79	12·66	12·73				
Bu	4	270—271°/2·0	116—118°	65	16·38	16·36				
Bu	5	259°/0·75	106—107°	57	15·75	15·75				
Bu	6	279—281°/0·9	110—111°	61	15·29	15·23				
Et	4	181—182°/0·25	111—112°	41	23·26	23·30				
Me	4	219—222°/0·35	204—205°	36	29·03	29·48	45·5	45·7	9·4	9·6
Me	5	249—252/1·3	167—168°	67	27·11	27·59	48·0	48·2	9·6	9·9
Me	6	217°/0·35	179—180°	50	26·43	25·98	49·9	50·1	10·1	10·2

The tetramethyl members differed from the others in their very limited solubility in hydrocarbons, such as benzene. For this reason it was impossible to determine their apparent molecular weight in this solvent. Tetramethylenebis(dimethylphosphine oxide) was obtained directly after the vacuum-distillation or recrystallization from a large volume of dry benzene. Crystallization of this substance from benzene–ethanol gave a crystalline product which contained ethanol (Found: P, 21·1. Calc. for $C_8H_{20}O_2P_2$,2EtOH: P, 20·5%). The product gave an enhanced molecular weight (413) determined ebullioscopically in acetone, which was much higher than that calculated (302) for the dialcoholate. In view of the numerous enhanced molecular weights found ebullioscopically in this group, it appears that considerable association of the dioxides occurs in solution. It was necessary to sublime this particular dioxide in a high vacuum at ~190° in order to remove the alcohol of crystallization. This gave a product identical with that obtained by the direct distillation. Pentamethylenebis(dimethylphosphine oxide) behaved similarly, yielding an adduct with ethanol (Found: P, 20·3. Calc. for $C_9H_{22}O_2P_2$,2EtOH: P, 19·6%). The tetramethylene member was most prone to form such adducts, since the hexamethylene member, which melted at 152—155° after recrystallization from ethanol, required but a single recrystallization from dry benzene to raise its m. p. to a constant value of 177—178°, before distillation. The ebullioscopic molecular weight of this substance in acetone was nearly normal (Found: 261. Calc.: 238), indicating relatively little association.

The tendency to association among these substances may be illustrated by some ebullioscopic molecular-weight data. The tetrabutyl members gave the following values which appear to indicate relatively little intermolecular association for $x = 4$, but considerable association for higher values: $x = 4$, M in benzene = 384 (calc., 378); $x = 5$, M in benzene = 461, in acetone = 831 (calc., 392·5); $x = 6$, M in benzene = 650, in acetone = 628, in camphor (Rast) = 504 (Calc., 406·5).

Except for the tetramethyl members, the compounds of this group were not appreciably hygroscopic in normal air. The solvent-free members of the tetramethyl group, and particularly the tetra- and the penta-methylene member, were hygroscopic and required drastic drying for the removal of moisture after an exposure; this appeared to be similar to the ethanol retention cited above.

Some of the microanalytical determinations were performed by the Galbraith Laboratories, Knoxville, Tenn., U.S.A. This work was supported by a grant from the National Science Foundation, Washington, D.C., U.S.A.

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795. *The Thermal Isomerization of* 1,1-*Dimethylcyclopropane.*

By M. C. Flowers and H. M. Frey.

The thermal isomerization of 1,1-dimethylcyclopropane has been investigated between 447° and 511° c. In this range, in an " aged " reaction vessel, the isomerization is homogeneous and unimolecular. The main products of the isomerization are 3-methylbut-1-ene and 2-methylbut-2-ene which are formed in nearly equal amounts. The first-order rate constant begins to decrease at a pressure of about 4 mm., and at 0·1 mm. it has fallen to 70% of the high-pressure value. A mechanism similar to that suggested for the isomerization of cyclopropane is consistent with the products formed and with the *A* factor for this reaction.

Experimental

Preparation of 1,1-*Dimethylcyclopropane.*—(*a*) 1,3-Dibromo-2,2-dimethylpropane was prepared from 2,2-dimethylpropane-1,3-diol in a manner similar to that of Shortridge *et al.*[1] A purer final product could be obtained by extraction of the crude product with concentrated sulphuric acid, followed by washing with aqueous sodium carbonate and water, before drying and fractional distillation. The overall yield was 42%.

(*b*) 1,3-Dibromo-2,2-dimethylpropane was cyclised by the method of Shortridge *et al.*[1] The 1,1-dimethylcyclopropane was freed from olefins (the major impurities) by prolonged contact at 0° with a 1% solution of potassium permanganate in saturated sodium hydrogen carbonate. The dimethylcyclopropane was distilled from this mixture into a trap cooled to −78°. Distillation at −78° into a trap cooled in liquid oxygen removed water, and the final product, obtained by fractional distillation under reduced pressure at −24° in a 13 in. Podbielniack column, contained <1% of total impurity.

Nitric oxide, prepared from " AnalaR " concentrated sulphuric acid and saturated sodium nitrate solution in presence of mercury, was condensed and stored in a liquid-oxygen trap.

Carbon dioxide, from the commercial solid was subjected to two trap-to-trap distillations (−78° to −186°) to remove water and non-condensable gases.

Apparatus.—A conventional " static " apparatus was used. Most isomerizations were carried out in a cylindrical silica reaction vessel (volume 205 ml.) fitted with a thermocouple well. In a few runs a reaction vessel packed with silica tubes (volume 139 ml.) was employed. The temperature was measured by use of a platinum/platinum–rhodium thermocouple calibrated against a standard platinum resistance thermometer. By using a furnace with a graded winding tapped at two points for external shunts the temperature gradient over the entire reaction vessel was kept to less than 0·5°. The temperature of the furnace, controlled by a Sunvic RT2 regulator, could be maintained indefinitely to within 0·2°.

Procedure.—1,1-Dimethylcyclopropane was admitted to the reaction vessel from a series of graduated gas pipettes. After each run the reaction vessel was opened to a 100 ml. evacuated bulb cooled in liquid oxygen. Between runs the reaction vessel was pumped down to 10^{-5} mm. Before any series of runs the vessel was " aged " by the addition of 100 mm. of the cyclopropane and allowing this to remain in the vessel for 36 hr. With a reaction vessel not so " aged " the rates were faster and not reproducible.

Analysis.—Reaction products were analysed by gas chromatography in a 30 ft. × 0·17 in. (i.d.) coiled copper column packed with hexane-2,5-dione on firebrick (30—60 mesh) with an additional 4 ft. (0·17 in. diam.) glass column packed with silver nitrate in ethylene glycol on a similar support. Both columns were at 0°. Hydrogen was the carrier gas. For the analysis of the runs at 100 mm. pressure and those in the packed reaction vessel, a Pye platinum-filament katharometer was used. All the other runs were analysed with a Gow-Mac (tungsten filament) katharometer. The silver nitrate–ethylene glycol column was necessary to separate the 1,1-dimethylcyclopropane and 3-methylbut-1-ene which are otherwise eluted at the same time.[2] The column was calibrated with synthetic mixtures of the products and reactant, equivalent to varying percentage decompositions. Determination of the percentage decomposition could be

[1] Shortridge, Craig, Greenlee, Derfer, and Boord, *J. Amer. Chem. Soc.*, 1948, **70**, 946.
[2] Frey, *Nature*, 1959, **183**, 743.

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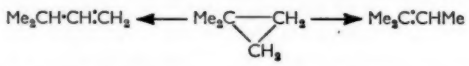
estimated to ±2% but the determination of the ratio of the products was less accurate (5%). Corrections were made throughout for " dead space " in capillaries and for impurities.

Results and Discussion

In the temperature range investigated (447—511°) 1,1-dimethylcyclopropane undergoes a first-order isomerization to give principally 3-methylbut-1-ene and 2-methylbut-2-ene in nearly equal amounts. In addition small amounts (approximately 1%) of 2-



methylbut-1-ene were formed. Simultaneously with the isomerization there was a small amount of thermal " cracking " which increased relative to the isomerization at the higher temperatures and higher percentage deompositions. The main products of the " cracking " reaction were ethane, ethylene, propane, and propene, and the total of the " cracking " compounds was less than 1% of the products of isomerization. Later experiments showed that these products could be accounted for almost entirely by the secondary decompositions of the primary isomerization products.

Preliminary runs at 490° with various pressures of dimethylcyclopropane in the range 550—6 mm. showed that in this pressure region the rate constant for the isomerization was independent of the pressure. Detailed studies were therefore carried out at 100 mm. pressure at 7 temperatures between 447° and 511°. At each, at least 8 runs were carried out in which the decomposition varied between 10 and 60%. Plots of the logarithm of the percentage of 1,1-dimethylcyclopropane against time were linear. No pressure change was observable on a simple mercury manometer during the reaction, in agreement with the small amount of cracking products formed.

The first-order rate constants are shown in Table 1. An Arrhenius plot gave a good

Table 1. *Rate constants for the isomerization of* 1,1-*dimethylcyclopropane.*

Temp.	447·3°	455·2°	463·0°	477·6°	485·8°	501·1°	511·3°
10^4k (sec.$^{-1}$)	1·14	1·82	2·94	6·56	10·1	24·2	40·4

straight line, and the frequency factor and energy of activation were calculated by the method of least squares, whence

$$k = 10^{15\cdot05} \exp(-62{,}600/\boldsymbol{R}T) \text{ sec.}^{-1}$$

The statistical probable error was only a few calories which merely indicates that the results are highly reproducible. The greatest uncertainty arises over the mean temperature of the reaction vessel, which can safely be assumed to be less than ±0·3° from the measured temperature. This would introduce a maximum uncertainty in the energy of activation of ±600 cal.

The thermal isomerizations of 3-methylbut-1-ene, 2-methylbut-2-ene, and 2-methylbut-1-ene (the initial products of the isomerization of dimethylcyclopropane) were briefly investigated so that the initial ratio of the products of the isomerization could be calculated with allowance for their own reactions. These compounds all isomerized more rapidly than they underwent thermal " cracking," though the " cracking " products were present in sufficient quantities to suggest that almost none were formed from the dimethylcyclopropane directly. Unlike the isomerization of 1,1-dimethylcyclopropane, the rates of isomerization of these compounds were strongly pressure-dependent in the range 12—100 mm. The corrections to be applied as a result of these experiments were small under all conditions. The corrected values are shown in Table 2.

The accuracy with which these ratios could be determined was not sufficient to decide definitely whether there is a difference in the energy of activation for the isomerization of dimethylcyclopropane to 3-methylbut-1-ene and 2-methylbut-2-ene. If there is a

difference it is not greater than 500 cal. mole^{-1}. In the case of the formation of 2-methylbut-1-ene, the quantities formed are so small that very large percentage errors are possible in the experimental value of the energy of activation and a value of as high as 68,000 cal. mole^{-1} is not inconsistent with the experimental data.

TABLE 2. *Primary ratios of isomerization products.*

Temp.	3-Methylbut-1-ene	2-Methylbut-2-ene	2-Methylbut-1-ene	Temp.	3-Methylbut-1-ene	2-Methylbut-2-ene	2-Methylbut-1-ene
447·3°	1	0·95	0·013	477·6°	1	0·95	0·015
455·2	1	0·93	0·013	485·8	1	0·96	†
463·0	1	0·94	0·018	501·1	1	0·98	†
477 *	1	0·96	0·023	511·3	1	0·98	0·018

* Packed reaction vessel.
† A very large scatter in these experimental values makes the average value unreliable.

All rate data refer to reaction vessels that had been " aged." If a clean reaction vessel was used the rate of isomerization of dimethylcyclopropane for the first run was at

FIG. 1.

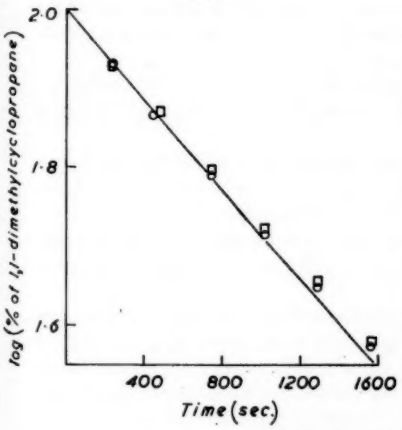
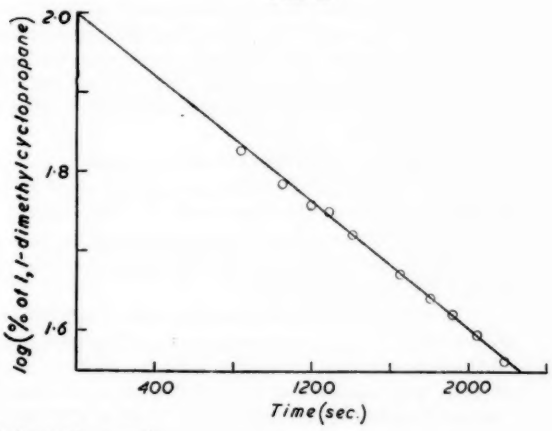


FIG. 2.



Solid curve, unpacked reaction vessel.
○, Packed reaction vessel.
□, Packed reaction vessel, with 10% of nitric oxide.

least twice that for an " aged " vessel. This increase in rate could be accounted for almost entirely by the additional production of 3-methylbut-1-ene. It thus appears that on a clean silica surface there is a heterogeneous reaction leading to this. To ensure that the rate constants obtained for the " aged " reaction vessels were for the homogeneous reaction only, a series of runs were carried out at 477° in a packed reaction vessel whose surface: volume ratio was 9·7 times that of the unpacked vessel. The rate plot obtained is shown in Fig. 1. The rate constant in the packed vessel is slightly *less* than that for the unpacked vessel and this can be accounted for by a drop of slightly less than 1° in the temperature. Since no thermocouple well was provided in the packed reaction vessel this temperature difference could not be checked. The packed vessel had a somewhat different geometry from the unpacked one, and this temperature difference is within the possible experimental errors.

Several runs were carried out at 477° in the packed reaction vessel with 100 mm. of 1,1-dimethylcyclopropane and about 11 mm. of nitric oxide (Fig. 1). Nitric oxide had no inhibitory effect; indeed it caused a small increase in the rate.

Since the isomerization in an " aged " reaction vessel appeared to be homogeneous,

was of first order over a large pressure range, and was not retarded by nitric oxide, it was considered probable that the reaction was a true unimolecular transformation. The rate of such transformations must show a pressure-dependence if the pressure is lowered sufficiently. By analogy with the pressure at which the first-order rate constant of the thermal isomerization of cyclopropane begins to decrease, as compared with the pressure at which excited cyclopropane, formed by the addition of methylene to ethylene, begins to isomerize, it is possible to estimate crudely the pressure at which the first-order rate constant for the thermal isomerization of dimethylcyclopropane should commence to fall, from the data on the excited molecule formed by the addition of methylene to isobutene,[3-6] to be *ca.* 3 mm. Accordingly runs were carried out below 6 mm. down to 0·1 mm. The values of the rate constants obtained are shown in Table 3. From a plot of the logarithm of the rate constant against the logarithm of the pressure it appears that the rate constant begins to decrease at approximately 4 mm.

TABLE 3. *Rate constants of isomerization at* 477·6°.

Pressure (mm.)	100	7·4	0·9	0·48	0·2	0·1
10^4k (sec.$^{-1}$)	6·56	6·56	6·09	5·73	5·18	4·66

At the very lowest pressures it was necessary to allow a reasonable percentage of the dimethylcyclopropane to isomerize before even the first point on the rate curve could be obtained, in order that sufficient products were present for accurate analysis. Thus, at 0·1 mm. the isomerization was only followed from 23 to 54% completion; however, the results (Fig. 2) were sufficiently precise to enable a reasonably accurate rate constant to be computed.

The ratio of the products did not appear to change significantly as the pressure was lowered. 2-Methylbut-1-ene was not detected in the runs at 0·1 mm. because the peak height would be of the same order as the " noise " of the katharometer. A *precise* ratio of the products could not be obtained for the low-pressure runs as the rates of isomerization of the primary products were not determined at low pressures (and these rates were highly pressure-dependent).

The apparatus was not designed for use with small amounts of dimethylcyclopropane in the presence of a large excess of non-condensable gas, and even at 0·1 mm. the fall-off of the rate constant compared with the high-pressure value is still small, so only one series of runs was carried out on the low-pressure isomerization in the presence of inert gas, carbon dioxide. Runs were carried out at 477° with 0·2 mm. of 1,1-dimethylcyclopropane and 3 mm. of carbon dioxide. The rate constant was $5{\cdot}84 \times 10^{-4}$ sec.$^{-1}$. In the absence of carbon dioxide it is $5{\cdot}07 \times 10^{-4}$ sec.$^{-1}$ at 0·2 mm. Thus the presence of carbon dioxide helps towards maintaining the Maxwell–Boltzmann distribution of energy. On a pressure-to-pressure basis carbon dioxide is approximately 0·13 times as effective as the dimethylcyclopropane itself. On a collision-to-collision basis, the ratio of the collision diameters of the dimethylcyclopropane to carbon dioxide being assumed to be 2 : 1, carbon dioxide is 0·26 times as effective.

From these results it appears most probable that the thermal isomerization of 1,1-dimethylcyclopropane is a true unimolecular reaction. In the Slater treatment of the isomerization of cyclopropane[7] the critical co-ordinate in the transition state is taken to be the distance between any hydrogen atom and any carbon atom to which it is not bound. The dimethylcyclopropane isomerization may be treated similarly. Thus rearrangement would be expected to take place when the distance between any of the four hydrogen atoms directly attached to the cyclopropane ring and a carbon atom in the ring to which they were not bonded became smaller than a critical value. Shifts of hydrogen atoms on

[3] Frey, *J. Amer. Chem. Soc.*, 1957, **79**, 1259.
[4] Prichard, Sowden, and Trotman-Dickenson, *Proc. Roy. Soc.*, 1953, *A*, **217**, 563.
[5] Knox, Trotman-Dickenson, and Wells, *J.*, 1958, 2897.
[6] Frey, *Proc. Roy. Soc.*, 1959, *A*, **250**, 409.
[7] Slater, *Proc. Roy. Soc.*, 1953, *A*, **218**, 224.

carbon atom 2 to carbon atom 3 or *vice versa* will result in the isomerization to 2-methylbut-2-ene. Shifts of these hydrogen atoms to carbon atom 1 will result in the transformation to 3-methylbut-1-ene. The closely similar yields of these two products makes it clear that these shifts must have closely similar probabilities. In the Slater treatment the most important factors governing the magnitude of the "*A*" factor for the cyclopropane isomerization are the high symmetry of the molecule (leading to twelve equivalent critical co-ordinates) and the values of the vibration frequencies of the carbon–hydrogen bonds. While no vibrational analysis for the dimethylcyclopropane molecule is available it seems likely that the carbon–hydrogen frequencies of the methylene groups in this molecule cannot differ appreciably from their values in cyclopropane. Accordingly one would expect that the "*A*" factor for the isomerization of the cyclopropane would be 1·5 (12/8) times as great as the "*A*" factor for this reaction. The actual experimental ratio is 1·3 which (the probable errors being considered) is in excellent agreement with this value.

The formation of the small quantities of 2-methylbut-1-ene is thought to proceed through a transition state whose critical co-ordinate is the distance between a hydrogen atom on either of the methyl groups and either carbon 2 or carbon 3. Since in the normal equilibrium configuration of the molecule this length is greater than the corresponding length in the transition states leading to the other isomerization products it is perhaps not surprising that little of the reaction proceeds *via* this path.

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THE UNIVERSITY, SOUTHAMPTON. [*Received, June 10th,* 1959.]

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796. *Steric Effects in Di- and Tri-arylmethanes. Part I. Electronic Absorption Spectra of* o-*Methyl Derivatives of Michler's Hydrol Blue and Crystal Violet; Conformational Isomers of Crystal Violet.*

By C. C. BARKER, M. H. BRIDE, and A. STAMP.

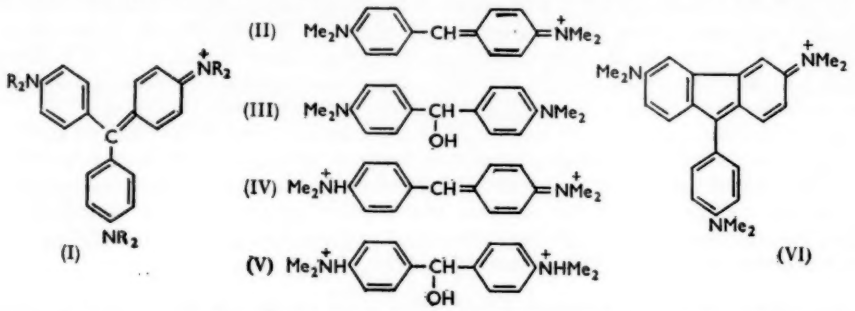
The first frequency absorption bands of *o*-methyl derivatives of Michler's Hydrol Blue and Crystal Violet show the expected reductions in frequency and intensity owing to the enforced rotation of the aryl rings.

The conformation of the 2,6-dimethyl derivative of Crystal Violet is discussed, and evidence against the existence of a conformational isomer of Crystal Violet is given.

THE introduction of an *ortho*-substituent into a triarylmethane dye invariably alters its molecular conformation and thereby alters its electronic absorption spectrum. A similar effect is produced by a *meta*-substituent when it is adjacent to a terminal dimethylamino-group, so that steric factors must exert an important influence upon the spectra of these dyes. However, the published spectra of sterically hindered charge resonance systems relate almost entirely to the heterocyclic cyanines; hindered trinuclear cyanines do not appear to have been studied, and very little attention has been given to the effect of crowding substituents upon di- and tri-arylmethane dyes. The present study was therefore initiated.

Scale drawings show that the *ortho*-hydrogen atoms in a triarylmethane dye overlap considerably, and the simplest assumption is that the shape of a structurally symmetrical dye, such as Crystal Violet (I; R = Me) or Pararosaniline (I; R = H), resembles that of a three-bladed propellor. In a diphenylmethane dye, however, the benzene rings may well be more nearly coplanar because overlap of the *ortho*-hydrogen atoms (Fig. 1) can be minimised by an increase in the phenyl–carbon–phenyl bond angle. *ortho*-Substituents

modify the spectra of these dyes by increasing the departure from molecular uniplanarity and by donating or withdrawing electrons. The work of Brooker *et al.*[1] leads to the prediction that the steric response of an electronically symmetrical dye such as Michler's Hydrol Blue (II) or Crystal Violet should be a bathochromic shift and a reduction in the intensity of the first frequency absorption band, and this prediction is supported by recent theoretical treatment.[2] Also, it has been shown that the effect of an electron-donating *ortho*-substituent is hypsochromic whereas the effect of an electron-withdrawing *ortho*-substituent is predicted to be bathochromic.[3] Thus the steric and electronic effects are



opposed when an *o*-methyl group is introduced, and this fact assists analysis of the resultant spectral shift and led to the frequent use of the methyl group in this study.

Because of the difficulty of purifying the colour salts of these dyes, the dye bases or their methyl ethers were isolated and converted into the colour salts for the spectra determinations by using an acidic solvent. Of the common solvents, water is unsatisfactory because it tends to promote molecular aggregation of this type of dye and thus produce an abnormal spectrum, but ethanol or acetic acid gives essentially monomeric solutions, and the latter solvent is sufficiently acidic to convert the dye bases or their methyl ethers into the colour salts without the addition of mineral acid. In acid solution, Michler's Hydrol Blue could exist as the base (III) (or monoprotonated base), the univalent cation (II), and the bivalent cations (IV) and (V). In order to obtain significant values of $\varepsilon_{max.}$ for the univalent cation, the acidity must be so adjusted that the concentrations of other forms of the dye are negligible, and it is assumed that the high and constant value of $\varepsilon_{max.}$ (147,500) obtained with acetic acid solutions containing from 98 to 95% of water indicates that this condition is fulfilled; lower values of $\varepsilon_{max.}$ are obtained when the water content of the acetic acid falls outside this range. Acetic acid containing 2% of water was therefore used as the standard solvent in these spectra determinations. The bases of Crystal Violet and Malachite Green form univalent cations which are stable over a wider range of pH than is Michler's Hydrol Blue, as is shown by the pK_b values (9·36, 6·90, and 5·61, respectively) obtained by Goldacre and Philips.[4]

The *ortho*-positions of Michler's Hydrol Blue are not equivalent (Fig. 1) and it is assumed that *ortho*-substituents take up less hindered "outside" positions. Molecular models suggest that an "outside" methyl group may not distort the molecule as the overlap of this group with the central hydrogen atom, shown in Fig. 1, is obviated by the overlap of the "inside" hydrogen atoms, but the 2-methyl derivative of Michler's Hydrol Blue shows a bathochromic shift and a reduction in the intensity of the first frequency absorption band, and this effect is increased in the 2,2'-dimethyl derivative (Table). These steric effects suggest that the molecule of Michler's Hydrol Blue approaches uniplanarity as a

[1] Brooker, White, van Zandt, Dent, and Sprague, *Chem. Rev.*, 1947, **41**, 325.
[2] Dewar, "Steric Effects in Conjugated Systems," Ed. G. W. Gray, Butterworths Scientific Publications, 1958, p. 46.
[3] Dewar, *J.*, 1950, 2329.
[4] Goldacre and Phillips, *J.*, 1949, 1724.

Absorption spectra of methyl derivatives of Crystal Violet and Michler's Hydrol Blue as 10^{-5}M-solutions in 98% acetic acid.

Compound	Absorption maxima (mμ) ($10^{-4}\varepsilon$ in parentheses)	Compound	Absorption maxima (mμ) ($10^{-4}\varepsilon$ in parentheses)
Crystal Violet substituents		*Michler's Hydrol Blue substituents*	
None	589(11·7); 305(2·6)	None	607·5(14·8)
2-Methyl	597(11·0); 305·5(2·3)	2-Methyl	614·5(13·0)
2,2′-Dimethyl	605(10·3); 308(2·3)	2,2′-Dimethyl	623(12·1)
2,2′,2″-Trimethyl	614(10·0); 309(2·1)	2,2′,6,6′-Tetramethyl	649(5·5)
2,6-Dimethyl	616(11·2)		
2,6-Dimethyl *	626·5		

* In toluene containing 0·1% of 2-naphthol.

result of an increase in the phenyl–carbon–phenyl bond angle, an increase which brings the two " outside " *ortho*-carbon atoms closer together. The first frequency absorption band of the 2,2′,6,6′-tetramethyl derivative shows a much larger bathochromic shift and reduction in intensity (Table) owing to the interaction of the two " inside " methyl groups.

FIG. 1.

[Reproduced, with permission, from "Steric Effects in Conjugated Systems," Ed. Gray, Butterworths, London, 1959, p. 37.]

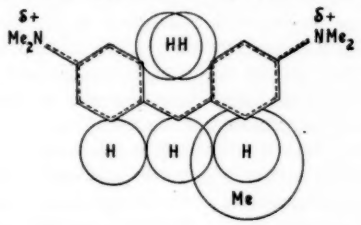


FIG. 2. *Absorption spectra of* (1) 10^{-5}M *solutions of Crystal Violet and its* (2) *2-methyl*, (3) *2,2′-dimethyl*, (4) *2,2′,2″-trimethyl derivative in* 98% *acetic acid.*

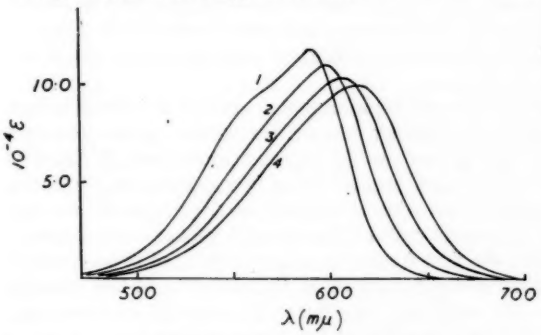
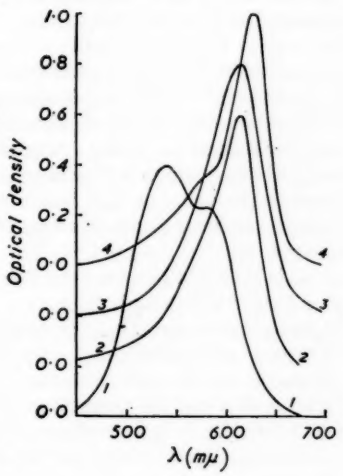


FIG. 3. *Absorption spectra of* (1) *Crystal Violet* (10^{-3}M) *in water, and its 2,6-dimethyl derivative in* (2) *water* (10^{-3}M), (3) 98% *acetic acid* (10^{-5}M), *and* (4) *toluene containing* 0·1% *of 2-naphthol* (10^{-5}M). *Maximum values of the optical density have been adjusted to* 1·0 *in each case.*



The 2-methyl, 2,2′-dimethyl, and 2,2′,2″-trimethyl derivatives of Crystal Violet show progressive bathochromic shifts and reductions in intensity of the first and second frequency absorption bands (Table), and the uniformity of the shift per methyl group of the long-wavelength band suggests that the rotational adjustment necessary to accommodate the *o*-methyl groups is shared uniformly between the aryl rings. However, the 2,6-dimethyl derivative shows a much larger bathochromic shift per methyl group and a relatively high absorption intensity (Table); these properties are consistent with the presence of a highly twisted dimethylaminoxylyl ring from which charge is concentrated onto the two dimethylaminophenyl rings. Also, the shoulder at about 540—550 mμ in the first frequency

absorption band of Crystal Violet is smaller in the spectra of the 2-methyl, 2,2′-dimethyl, and 2,2′,2″-trimethyl derivatives (Fig. 2) and is completely absent from the spectrum of the 2,6-dimethyl derivative (Fig. 3).

Lewis, Magel, and Lipkin [5] attributed this shoulder given by Crystal Violet in organic solvents or in dilute aqueous solution (10^{-5}M) to the presence of a conformational isomer in which one of the dimethylaminophenyl groups is rotated in the opposite sense to that of the other two rings. However, in more concentrated aqueous solution (10^{-3}M) the molecules of Crystal Violet aggregate and give rise to a first frequency absorption band in which the normal peak at 598 mμ has become subsidiary to a peak at 540 mμ,[6] the position of the shoulder when the Crystal Violet is in organic solvents or in dilute aqueous solution (Fig. 3). Lewis *et al.* were aware of this fact but assumed that aggregation did not occur in organic solvents. The shoulder is also much exaggerated in a toluene solution of Crystal Violet, and Lewis *et al.* attributed this to an increase in the proportion of unsymmetrical conformational isomer.

Because the highly twisted dimethylaminoxylyl ring of the 2,6-dimethyl derivative of Crystal Violet would prevent face-to-face aggregation of the molecules, the absence of shoulder from the first frequency absorption band of this derivative suggests that the shoulder in that of Crystal Violet should more properly be attributed to the presence of aggregated dye molecules. This band of the 2,6-dimethyl derivative is also free from shoulder when observed in concentrated (10^{-3}M) aqueous solution, but a distinct shoulder is given by the dye in toluene (Fig. 3). Thus, it seems likely that toluene is an aggregating solvent, and this is confirmed by a study of the absorption spectrum of the fluorene analogue of Crystal Violet (VI), in which the planarity of the fluorene nucleus [7] permits the dye to aggregate readily but prohibits the existence of a conformational isomer. In 95% alcohol, the dye is monomeric and the green solution gives a single absorption band ($\lambda_{max.}$ 647 mμ) [8] in the visible region, whereas in water the dye (10^{-5}M) is largely aggregated and the blue solution shows a band ($\lambda_{max.}$ 590 mμ) in which the monomeric dye is represented only by a small shoulder. A solution of the dye in toluene is also blue and gives a band ($\lambda_{max.}$ 616 mμ) which is devoid of shoulder and which must be due to aggregated molecules because the value of $\lambda_{max.}$ is less than that of the monomeric band obtained in ethanol; toluene produces a bathochromic shift of the monomer bands of this type of dye (see Table and ref. 5).

It is likely that an unsymmetrical conformational isomer of Crystal Violet would absorb at a longer wavelength than its symmetrical isomer because the former would contain a highly rotated dimethylaminophenyl group and would thus resemble the 2,6-dimethyl derivative of Crystal Violet. On the other hand, bands arising from aggregated molecules should become more intense at lower temperatures because of increased aggregation, whereas Lewis *et al.* found the anomalous absorption of Crystal Violet to decrease as the temperature was lowered. It is now observed that the first frequency absorption band of an aqueous solution of Crystal Violet (10^{-4}M) shows a slight decrease in the intensity of the shoulder when the temperature is raised from 20° to 60°, and it seems that some other explanation must be found for the disappearance of the shoulder at low temperatures.

The derivatives of Michler's Hydrol Blue were prepared by reduction of the corresponding ketones in ethanol with sodium amalgam, and pure hydrols were readily obtained, whereas oxidation of the corresponding derivatives of diphenylmethane to hydrols was found to be impracticable when *ortho*-substituents were present. *NN*-Dimethyl-*m*-toluidine and carbonyl chloride in the presence of zinc chloride gave 4,4′-bisdimethylamino-2,2′-dimethylbenzophenone as pale-yellow crystals, m. p. 96°, without difficulty; Fierz and Koechlin [9] claim to have prepared this ketone as colourless crystals, m. p. 196°,

[5] Lewis, Magel, and Lipkin, *J. Amer. Chem. Soc.*, 1942, **64**, 1774.
[6] Holmes, *Ind. Eng. Chem.*, 1924, **16**, 36.
[7] Burns and Iball, *Proc. Roy. Soc.*, 1955, *A*, **227**, 200.
[8] A. Barker and C. C. Barker, *J.*, 1954, 1307.
[9] Fierz and Koechlin, *Helv. Chim. Acta*, 1918, **1**, 223.

by the action of carbon tetrachloride on *NN*-dimethyl-*m*-toluidine in the presence of aluminium trichloride, but attempts to repeat their preparation gave only the 2,2′,2″-trimethyl derivative of Crystal Violet. Interaction of carbonyl chloride, *NN*-dimethyl-3,5-xylidine, and zinc chloride gave a mixture of 4,4′-bisdimethylamino-2,2′,6,6′-tetramethylbenzophenone and 2,4′-bisdimethylamino-2′,4,6,6′-tetramethylbenzophenone which required chromatographic separation. Reduction of the latter with sodium amalgam gave a hydrol which did not develop colour with acetic acid, showing that the original ketone contains at least one dimethylamino-group adjacent to the carbonyl group. Failure to isolate a third isomeric ketone is evidence that the initial condensation with carbonyl chloride gave only 4-dimethylamino-2,6-dimethylbenzoyl chloride, in which case the ketone which failed to form a colour salt on reduction must have the structure given. The initial formation of an isomeric acid chloride would have led, most probably, to the formation of a third ketone, *viz.*, 2,2′-bisdimethylamino-4,4′,6,6′-tetramethylbenzophenone.

The unsymmetrical 4,4′-bisdimethylamino-2-methylbenzophenone was readily prepared from *p*-dimethylaminobenzoyl chloride and *NN*-dimethyl-*m*-toluidine in the presence of zinc chloride, but attempts to condense *p*-dimethylaminobenzoyl chloride or its *o*-methyl derivative with *NN*-dimethyl-3,5-xylidine gave anomalous products which were not identified.

The 2-methyl derivative of Crystal Violet was prepared from Michler's ketone and *NN*-dimethyl-*m*-toluidine in the presence of phosphorus oxychloride, and it was isolated and purified as the dye base. The 2,6-dimethyl derivative of Crystal Violet was obtained in a similar way from *NN*-dimethyl-3,5-xylidine, but the colour salt gave a red product, believed to be essentially 4′,4″-bisdimethylamino-2′,6′-dimethylfuchsone, when treated with alkali, and the dye was isolated as the perchlorate.

The 2,2′-dimethyl derivative of Crystal Violet was obtained directly as the dye base by the action of *p*-dimethylaminophenyl-lithium on 4,4′-bisdimethylamino-2,2′-dimethylbenzophenone. The 2,2′,2″-trimethyl derivative was obtained as the colour salt from carbon tetrachloride and *NN*-dimethyl-*m*-toluidine in the presence of aluminium trichloride. Conversion of the colour salt to the dye base required treatment at room temperature with one equivalent of aqueous sodium hydroxide for 16 hours; use of an excess of sodium hydroxide gave a red product from which pure dye base could not be isolated. The formation of a red product is again associated with the presence of a highly hindered central carbon atom, but the tendency to form this type of product is less than in the case of the 2,6-dimethyl derivative of Crystal Violet.

The 2,2′,2″-trimethyl derivative of *leuco*-Crystal Violet, obtained from *NN*-dimethyl-*m*-toluidine and ethyl orthoformate, gave a blue solution when oxidised in acetic acid with lead dioxide but the dye base could not be isolated, and the condensation of *NN*-dimethyl-*m*-toluidine with 4,4′-bisdimethylamino-2,2′-dimethylbenzophenone in the presence of phosphorus oxychloride gave a small amount of the same *leuco*-compound as the only isolable product. The failure of the two latter methods must be attributed to the hindered nature of the central carbon atom in the required dye. A further anomalous reaction was encountered when attempting to repeat the preparation of the 2,2′,2″,6,6′,6″-hexamethyl derivative of *leuco*-Crystal Violet from *NN*-dimethyl-3,5-xylidine and ethyl orthoformate described by Noelting and Trautman;[10] the product was bis-(4-dimethylamino-2,6-xylyl)-methane.

Experimental

4,4′,4″-Trisdimethylamino-2-methyltriphenylmethanol.—Michler's ketone (1·0 g.), *NN*-dimethyl-*m*-toluidine (2·7 g.), and phosphorus oxychloride (1·0 g.) were heated in a sealed tube at 100° for 5 hr. The mixture was basified with aqueous potassium carbonate, excess of amine was removed by steam distillation, and the residue was crystallised from ethanol (70 c.c.), giving the *base* (0·75 g.), m. p. 170—173°, raised to m. p. 172—173° by recrystallisation once

[10] Noelting and Trautman, *Ber.*, 1891, **24**, 562.

from ethanol and then twice from benzene–light petroleum (b. p. 60—80°; 2 parts) (Found: C, 77·3; H, 8·3; N, 10·2. $C_{26}H_{33}ON_3$ requires C, 77·4; H, 8·2; N, 10·4%).

4,4′,4″-Trisdimethylamino-2,2′-dimethyltriphenylmethanol.—A portion (15 c.c.) of a solution of *p*-dimethylaminophenyl-lithium, prepared from 4-bromo-*NN*-dimethylaniline (5·0 g.), lithium (0·4 g.), and ether (45 c.c.), was run into 4,4′-bisdimethylamino-2,2′-dimethylbenzophenone (1·48 g.) in benzene (50 c.c.) contained in a flask flushed with dry nitrogen. The mixture was stirred at room temperature for 15 min, and then at 50° for 30 min., then water (100 c.c.) was added. The organic layer was dried (Na_2SO_4) and the solvent removed, yielding a blue gum which gave a pale blue solid (1·6 g.), m. p. 130—155°, after trituration with light petroleum (b. p. 40—60°; 10 c.c.). Three crystallisations from benzene–light petroleum (b. p. 60—80°; 2 parts) gave the *base* as very pale blue micro-crystals, m. p. 165—166° (Found: C, 77·8; H, 8·3; N, 10·3. $C_{27}H_{35}ON_3$ requires C, 77·7; H, 8·4; N, 10·1%).

Tris-(4-dimethylamino-2-tolyl)methanol.—Powdered aluminium trichloride (22·0 g.) was added to cooled *NN*-dimethyl-*m*-toluidine (18·8 g.); carbon tetrachloride (6·2 g.) was added dropwise to the resultant paste and the mixture was stirred at 30° for 5 hr. The green crystals which separated were washed with a little water, stirred with water (75 c.c.) containing concentrated hydrochloric acid (0·6 c.c.) for several hr., removed, and crystallised thrice from water giving the 2,2′,2″-trimethyl derivative of Crystal Violet (2·8 g.). The dye (2·0 g.) in water (250 c.c.) was stirred with water (10 c.c.) containing sodium hydroxide (0·9 g.) for 16 hr., and the precipitated base was removed and washed with water, and then stirred with ethanol (5 c.c.) to remove coloured impurities. This product, thrice crystallised from benzene–light petroleum (b. p. 60—80°) gave the dye *base* as colourless crystals, m. p. 205—206° (decomp.) (Found: C, 77·8; H, 8·6; N, 9·7. $C_{28}H_{37}ON_3$ requires C, 78·0; H, 8·6; N, 9·7%).

2,6-Dimethyl Derivative of Crystal Violet.—Michler's ketone (1·0 g.), *NN*-dimethyl-3,5-xylidine (2·4 g.), and phosphorus oxychloride (1·0 g.) were heated in a sealed tube at 100° for 5 hr., and the product was purified by repeated precipitation from aqueous solution by addition of sodium chloride. The resultant dye was finally precipitated as the sparingly soluble *perchlorate* (Found: C, 64·5; H, 7·2; N, 8·4. $C_{27}H_{34}O_4N_3Cl$ requires C, 64·9; H, 6·8; N, 8·4%).

4,4′-Bisdimethylamino-2-methyldiphenylmethanol.—4-Dimethylaminobenzoyl chloride (9·65 g.), prepared by Décombé's method,[11] anhydrous zinc chloride (2·1 g.), and *NN*-dimethyl-*m*-toluidine (16·3 g.) were stirred at room temperature for 1½ hr., then at 30° for 2 hr., at 55° for 18 hr., and finally at 80° for 2 hr. The mixture was basified with aqueous sodium hydroxide, excess of *NN*-dimethyl-*m*-toluidine was removed by steam distillation, and the residue was crystallised (charcoal) from ethanol to give pale green crystals (6·9 g.), m. p. 104—108°, unchanged by recrystallisation from ethanol. This product, by elution from an alumina column (190 × 17 mm.) in benzene and crystallisation of the first 3·4 g. of eluate from ethanol, gave *4,4′-bisdimethylamino-2-methylbenzophenone* as yellow crystals, m. p. 116° (Found: C, 76·4; H, 7·7; N, 9·8. $C_{18}H_{22}ON_2$ requires C, 76·6; H, 7·8; N, 9·9%). The aforementioned ketone (0·5 g.) in ethanol (30 c.c.) and water (1·5 c.c.) was stirred and refluxed with sodium amalgam (3% Na; 2·7 g.) for 2½ hr., more sodium amalgam (2·7 g.) being added after 1½ hr. The resultant solution was poured into water (150 c.c.) and the precipitate was washed with water, dried *in vacuo*, and crystallised from benzene–light petroleum (b. p. 40—60°), thereby giving *4,4′-bisdimethylamino-2-methyldiphenylmethanol* as colourless crystals, m. p. 79—80° (Found: C, 75·9; H, 8·8; N, 9·6. $C_{18}H_{24}ON_2$ requires C, 76·1; H, 8·5; N, 9·9%).

Bis-(4-dimethylamino-2-tolyl)methanol.—Carbonyl chloride (3·42 g.) was absorbed in cooled *NN*-dimethyl-*m*-toluidine (20·0 g.), and the mixture was stirred at room temperature for 17 hr., and then at 30° while anhydrous zinc chloride (1·38 g.) was added. The temperature was maintained at 30° for 3 hr., raised to 55° during 2 hr., then kept at 80—85° for 2 hr. The product was basified with dilute aqueous ammonia, excess of *NN*-dimethyl-*m*-toluidine was removed by steam distillation, and the residue was dissolved in benzene, and dried (Na_2SO_4), and the solution was passed through a short alumina column. Removal of the solvent and crystallisation of the residue from ethanol gave brownish-yellow crystals (2·4 g.), m. p. 92—94°. Sublimation of these crystals at 200° (bath)/10^{-4} mm., followed by recrystallisation from ethanol gave yellow crystals of *4,4′-bisdimethylamino-2,2′-dimethylbenzophenone*, m. p. 96° (Found: C, 76·9; H, 8·2; N, 9·4. $C_{19}H_{24}ON_2$ requires C, 77·0; H, 8·1; N, 9·5%). The aforementioned ketone was reduced with sodium amalgam as for the reduction of the monomethyl analogue and gave *bis-(4-dimethylamino-2-tolyl)methanol* as colourless crystals, m. p. 114° (from light

[11] Décombé, *Bull. Soc. chim. France*, 1951, 417.

petroleum, b. p. 60—80°) (Found: C, 75·9; H, 8·8; N, 9·3. $C_{19}H_{29}ON_2$ requires C, 76·5; H, 8·7; N, 9·4%).

Bis-(4-dimethylamino-2,6-xylyl)methanol.—Carbonyl chloride (3·3 g.) and *NN*-dimethyl-3,5-xylidine were allowed to react in the presence of zinc chloride as described for the preparation of 4,4′-bisdimethylamino-2,2′-dimethylbenzophenone, and the excess of *NN*-dimethyl-3,5-xylidine was removed by steam distillation. The crude product, which after one crystallisation from ethanol melted at 104—107° to a cloudy liquid which became clear at 125°, was eluted from a column of activated alumina (400 × 30 mm.) by a mixture of equal volumes of benzene and light petroleum (b. p. 60—80°) and then by benzene (4 vols.)–methanol (1 vol.) yielding the following fractions: F_1, 1·81 g., benzene–light petroleum (1945 c.c.); F_2, 0·48 g., benzene–light petroleum (1860 c.c.); F_3, 1·86 g., benzene–methanol (400 c.c.). Reduction of samples of these fractions with sodium amalgam and treatment of the products with acetic acid gave colourless, pale blue, and intense blue solutions from F_1, F_2 and F_3 respectively. Fraction F_1, twice crystallised from ethanol gave yellow crystals of *2,4′-bisdimethylamino-2′,4,6,6′-tetramethylbenzophenone*, m. p. 125—125·5° (Found: C, 77·5; H, 8·5; N, 8·7. $C_{21}H_{28}ON_2$ requires C, 77·8; H, 8·6; N, 8·6%). Fraction F_3, thrice crystallised from ethanol, gave *4,4′-bisdimethylamino-2,2′,6,6′-tetramethylbenzophenone* as yellow crystals, m. p. 165° (Found: C, 77·5; H, 8·7; N, 8·9%). The aforementioned ketone was reduced as for 4,4′-bisdimethylamino-2-methylbenzophenone and gave colourless crystals of *bis-(4-dimethylamino-2,6-xylyl)methanol*, m. p. 165—166° (from benzene–light petroleum) (Found: C, 76·6; H, 9·3; N, 9·0. $C_{21}H_{30}ON_2$ requires C, 77·3; H, 9·2; N, 8·6%).

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797. *Comparative Reaction Rates in Solid and in Liquid Sulphuric Acid–Water Mixtures.*

By T. G. BONNER and J. C. LOCKHART.

Rate constants of two different reactions have been measured in liquid and in solid sulphuric acid–water mixtures at 0°. The occurrence in both cases of a more rapid reaction in the solid medium is discussed.

During a study of rate measurements on the cyclodehydration of anils of acetylacetone to 2,4-dimethylquinolines [1] in sulphuric acid at temperatures below 10° it was found that where solidification of the medium inadvertently occurred the reaction still proceeded to completion. In consequence, a comparative study was made of the rates of this reaction in the solid and in corresponding supercooled liquid media at the same temperature, 0°,

TABLE 1. *Rate constants (min.$^{-1}$) at 0° in solid (k_S) and supercooled liquid (k_L) sulphuric acid–water mixtures.*

(*a*) Cyclodehydration of anils (0·025M)

Compound *	I	I	II	II
% H_2SO_4	85·5	84·0	85·5	84·0
10^4k_S	6·4, 6·2	3·4	0·93	0·72
10^4k_L ...	3·2, 3·0	1·7	0·47	0·31

(*b*) Denitration of nitroguanidines (0·0074M)

Compound *	III	III	III	IV
% H_2SO_4 ...	86·4	85·7	84·5	84·5
10^3k_S	7·15	6·72	5·23	5·80
10^3k_L	1·78	1·60	1·27	2·12

* I, 2-*p*-Toluidinopent-2-en-4-one; II, 2-anilinopent-2-en-4-one; III, 2-nitrimino-1,3-diazacyclopentane; IV, 4-methyl-2-nitrimino-1,3-diazacyclopentane.

with two anils, 2-*p*-toluidinopent-2-en-4-one and 2-anilinopent-2-en-4-one and two different acid–water mixtures. In all cases, the cyclodehydration in the solid media was approximately twice as fast as in the liquid medium (Table 1*a*). Rates in solid and in liquid sulphuric acid media of the denitration of nitroguanidines to guanidine and nitric acid [2] were compared similarly; those in the solid media were about four times greater

[1] Bonner, Thorne, and Wilkins, *J.*, 1955, 2351.
[2] Bonner and Lockhart, *J.*, 1958, 3852.

than in the liquid for both 2-nitrimino-1,3-diazacyclopentane and 4-methyl-2-nitrimino-1,3-diazacyclopentane as shown in Table 1*b*. Variation of the initial concentration of 2-nitrimino-1,3-diazacyclopentane did not markedly change the ratio k_S/k_L of the rate constants for the solid and the liquid state (Table 2). As these initial studies were confined

TABLE 2. *Denitration of 2-nitrimino-1,3-diazacyclopentane at different initial concentrations in 84·5% sulphuric acid at 0°.*

10^3 × Initial concn. (M)	0·74	0·89	2·90
10^3k_S (min.$^{-1}$)	5·13, 5·34, 5·23, 5·32	5·07	5·12
10^3k_L (min.$^{-1}$)	1·27	1·18	1·54

to measurements at 0° the sulphuric acid–water mixtures were restricted to the range 81—86% sulphuric acid over which the freezing points have values between 2 and 8°.[3] The only other range in which freezing points are above 0° is 98—100% sulphuric acid, but denitrations were too fast for measurement in these acids while the cyclodehydrations which proceeded at fast but measurable rates did not give satisfactory results, largely owing to the tendency of the solid samples to melt partially during reaction. Lower temperatures, *e.g.*, −10° to −20°, might avoid this difficulty, but will introduce the hazard of spontaneous solidification of the supercooled liquid.

A feature common to both the cyclodehydrations and denitrations is that they proceed through protonated forms of the substrate. In cyclodehydration this is a doubly charged species [4] which reacts by a rate-determining closure of the side chain to either *ortho*-position, followed by rapid loss of a proton. The medium is involved in maintaining the equilibrium concentration of the fractionally small amount of diprotonated anil and in the subsequent removal of the proton from the reaction intermediate, but both these proton transfers are presumably as fast in solid media as in the liquid and in any case are not rate-determining. The more rapid ring closure in a solid medium may then be due to entropy; the " caged " anil molecule has a very limited translatory motion but the greater flexibility of the side chain leads to a higher proportion of collisions with the *ortho*-positions at which the closure is affected. This effect would be similar to that discussed by Fairclough and Hinshelwood [5] for bimolecular reactions in solution where the solute molecule is larger than the solvent molecule and the solvent has a high density. Under these conditions the solvent can assume a close-packed structure from which the solute molecules tend to be squeezed out in groups with a consequent large increase in the number of repeated collisions between pairs of solute molecules at the expense of fresh encounters.

Although the denitration of nitroguanidines in sulphuric acid–water mixtures has a more complex mechanism than the cyclodehydration, it is basically similar in that the ionic form of the substrate requires assimilation of a second proton for reaction to occur. The transition state appears to require the presence of the solvent species,[2] H_3O^+ and HSO_4^-, which are involved only in proton transfer to, and proton withdrawal from, the bivalent nitroguanidinium ion during its conversion into the guanidinium and nitronium ion. A significant difference between the liquid and the solid environment could arise as a result of this participation of solvent acid and base species in the denitration. In the liquid the doubly positively charged nitroguanidinium ion will have a preponderantly negatively charged ionic atmosphere while, in the solid state, the solid phase in this range of media is the monohydrate [3] H_2O,H_2SO_4 (or H_3O^+,HSO_4^-) which provides the most favourable balance of the acid and base catalysts as the environment of the reacting ion.

Evidently the study of bimolecular reactions in solid sulphuric acid–water mixtures will provide results of even greater interest than the two reactions reported here. Some preliminary investigations on the nitration of guanidine using guanidine nitrate to provide

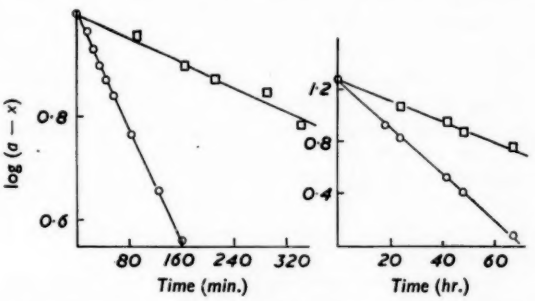
[3] Pickering, *J.*, 1890, 331.
[4] Bonner and Barnard, *J.*, 1958, 4176.
[5] Fairclough and Hinshelwood, *J.*, 1939, 593.

both reactants showed that the reaction was too fast for measurement even at 0° in the optimum range of sulphuric acid–water mixtures. The measurements did reveal, however, that the equilibrium was more rapidly attained in the solid than in the liquid medium.

Experimental

Materials and Media.—These were prepared as previously described.[1,2]

Kinetic Measurements.—For both cyclodehydration and denitration reactions, the reactant was weighed into a short tube made from a B24 cone. At zero time this tube was inserted into the neck of the flask containing the liquid sulphuric acid medium at 0° and shaken vigorously to dissolve the reactant as rapidly as possible. The flask was shaken in the bath at 0° for about 1 min. To ensure similarity of experimental conditions for both solid- and liquid-phase measurements, 2 ml. aliquot portions were successively removed without delay from the reaction solution and introduced into stoppered tubes, equal numbers of which were immersed in liquid air (to effect rapid solidification) and in a large vacuum flask containing ice and water. Each tube in the liquid-air bath was transferred to the ice-bath after complete solidification of the solution (which required about 1 min.) had occurred. In each experiment 5—8 samples each for the solid and liquid kinetic measurements were thus removed. At fixed time intervals, the stoppered tubes were taken from the ice-baths, and the contents diluted with water to stop further reaction and analysed in the usual way for the amount of unchanged reactant.[1,2] On rare occasions in the cyclodehydration, the supercooled sulphuric acid medium began to solidify during the initial mixing with the reactant. In such cases the experiment was repeated with the medium kept at about 5° before the addition of the reactant, and after complete dissolution of the latter the temperature of the solution was reduced rapidly to 0° by shaking for a few minutes in an ice-bath before removing the 2 ml. aliquot portions to the stoppered tubes. Since all reactions were extremely slow, this procedure did not introduce any detectable error.



A, Denitration of 2-nitrimino-1,3-diazacyclopentane in 85·7% sulphuric acid; B, cyclodehydration of 2-p-toluidinopent-2-en-4-one in 85·5% sulphuric acid.

□ Liquid, ○ solid medium.

Simkins and Williams [6] have shown that the reversible denitrations in liquid sulphuric acid can be treated as a simple first-order change up to about 20% conversion of the nitroguanidine, and this procedure was followed here of plotting log $(a - x)$ against time; for liquid media good straight lines were obtained up to about 20% conversion, and for reactions in the solid media the straight line plot continued up to 50% conversion of the nitroguanidine. The cyclodehydration reaction was followed up to about 80% conversion. Typical results are shown in the Figure.

Royal Holloway College, Englefield Green, Surrey. [*Received, June 19th*, 1959.]

[6] Simkins and Williams, *J.*, 1952, 3086; 1953, 1386.

798. *Steroids. Part XLIII.* Comparison of the 16-Bromo-17-ketones and 16-Bromo-17-alcohols in the 3-Unsubstituted and 3β-Oxygenated 5α-Androstane Series.*

By J. Fajkoš.

The differences which Shoppee, Jenkins, and Summers reported between the chemical behaviour of the 16-bromo-17-ketones and 16-bromo-17-alcohols of the 3-unsubstituted 5α-androstane series on the one hand and that of their 3β-methoxy- and 3β-acetoxy-derivatives on the other are shown not to exist.

In 1954, we reported[1] the steric course of the bromination of 17-keto-steroids at position 16 and the preparation and properties of the epimeric 16-bromo-3β-acetoxy- and 16-bromo-3β-methoxy-5α-androstan-17-ones, and a number of 16-bromo-17-hydroxy-derivatives. Later, the corresponding reactions and derivatives were described for the 5,6-unsaturated 3α- and 3β-hydroxy-series.[2]

Shoppee, Jenkins, and Summers[3] recently carried out analogous reactions with (3-unsubstituted) 5α-androstan-17-one (I), and characterise their results as "strikingly different" from ours. They give the principal differences as "the variation, with the nature of the 3β-substituent, (i) of the rate of epimerisation of the 16α-bromo-17-ketones as disclosed by the occurrence of retention, as opposed to inversion of configuration at $C_{(16)}$, on reduction with sodium borohydride in methanol at 20°, (ii) the position of the equilibrium amongst the three pairs of epimeric ketones, and (iii) the production of 16β,17β-epoxides" [from the (*trans*)-16α-bromo-17β-alcohols in our work, as contrasted with the formation of the 17-ketone in the corresponding experiment of Shoppee and his co-workers].

Some of these conclusions appear to spring from a misunderstanding of our work; but certain real differences remain. The explanation suggested to account for the differences—conformational effects induced by the presence of a 3β-substituent in ring A and transmitted, by the long-range conformational mechanism envisaged by Barton,[4] to positions 16 and 17 in ring D—appeared to us to be *a priori* improbable; in fact, sterically more incisive changes such as the change from 3β- to 3α-substitution or the introduction of a 5,6-double bond had been found[2] to have no appreciable effect of this type. We therefore undertook some further experimental studies, including a repetition of certain experiments of Shoppee, Jenkins, and Summers.

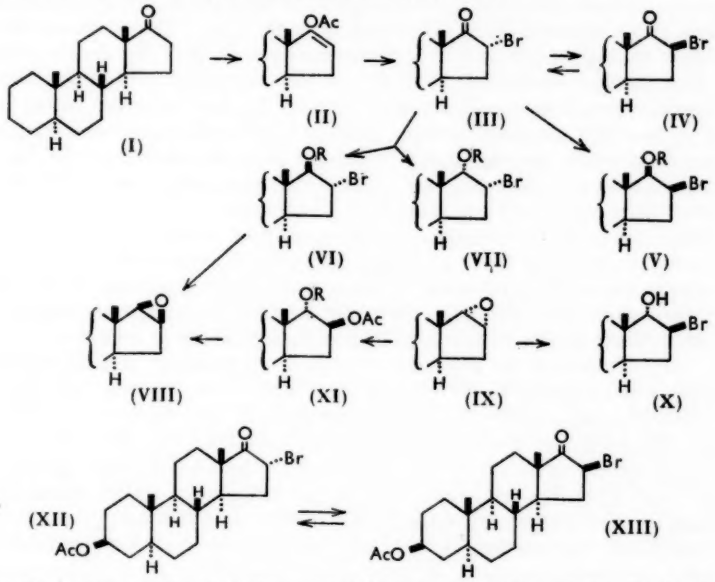
In their conclusion (i)—reduction of 16α-bromo-5α-androstan-17-one (III) with sodium borohydride without inversion at $C_{(16)}$, compared with extensive inversion in this reaction in the 3β-oxygenated series reveals differences in the rate of epimerisation of the starting bromo-ketones—Shoppee and his co-workers overlook the fact that their reaction was carried out in methanol–ether and ours in ethanol (misquoted[3] as methanol). We have previously stressed[1] how the solvent may influence critically the steric outcome of this reaction, and shown that, with lithium borohydride as the reagent, reduction of the 17-keto-group of the bromo-ketone (XII) proceeds with retention of configuration at $C_{(16)}$ in ether, but in ethanol gives a mixture of products epimeric at $C_{(16)}$. This alone accounts reasonably for the discrepancy noted by Shoppee, Jenkins, and Summers, but we have confirmed this explanation as follows:

Reduction of 16α-bromo-5α-androstan-17-one (III) [conveniently prepared by the

* Part XLII, *Coll. Czech. Chem. Comm.*, 1959, **24**, 1515.

[1] Fajkoš, *Chem. Listy*, 1954, **48**, 1800; *Coll. Czech. Chem. Comm.*, 1955, **20**, 312; 14th Internat. Conf. Union Pure Appl. Chem., Zurich, 1955.
[2] Fajkoš and Šorm, *Chem. Listy*, 1958, **52**, 505; *Coll. Czech. Chem. Comm.*, 1959, **24**, 766
[3] Shoppee, Jenkins, and Summers, *J.*, 1958, 3048.
[4] Barton, *Experientia*, 1955, Suppl. II, p. 121.

bromination of the enol acetate (II)] under the conditions used by Shoppee and his co-workers, *i.e.*, in methanol–ether (2 : 1), gave the bromohydrins (VI and VII; R = H) without epimerisation, but in ethanol the product was 16β-bromo-5α-androstan-17β-ol (V; R = H), identical with the material obtained by Shoppee, Jenkins, and Summers by a different route.[3] Sodium borohydride from three different commercial sources gave the same results, yields of the 16β-bromo-17β-alcohol (V; R = H) varying only between 64% and 70%. The supposed difference between the 3β-oxygenated and 3-unsubstituted series is thus illusory; it will be recalled that analogous behaviour was also shown by compounds of the 3α-substituted and 5,6-unsaturated series.[2]



Our earlier interpretation [1] had assumed that epimerisation at $C_{(16)}$ took place under the influence of the alkaline reagent before reduction of the keto-group; thus, 16α-bromo-3β-methoxy-5α-androstan-17-one, when kept in ethanolic sodium borohydride previously treated with acetone, gave the 16β-bromo-17-ketone in 40% yield; from its optical rotation, the crude product appeared to contain about 80% of the 16β-bromo-isomer. Shoppee, Jenkins, and Summers [3] exposed 16α-bromo-5α-androstan-17-one (III) to methanolic sodium hydroxide " equivalent to the alkalinity generated in reduction with sodium borohydride " and reported obtaining a product substantially free from bromine. We have examined the effect of acetone-treated sodium borohydride solutions and of 0·2% methanolic and ethanolic sodium hydroxide on Shoppee's 16α-bromo-5α-androstan-17-one (III) and on 3β-acetoxy-16α-bromo-5α-androstan-17-one (XII) as well as repeating our earlier experiments with the 3β-methoxy-derivative. In all these cases, the final optical rotation of the mixture corresponded to a content of about 75% of the 16β-bromo-17-ketone; the crude products contained the calculated amount of bromine, and on crystallisation yielded some of the pure 16β-bromo-epimerides. Since, moreover, the alkali-catalysed epimerisation at $C_{(16)}$ proved to be very rapid, the final rotation value being reached within 2 minutes, these results fully support our earlier interpretation [1] of the epimerisation during sodium borohydride reduction of the (thermodynamically labile) 16α-bromo-17-ketones. The *a priori* objection [3] that such a mechanism would also require the 16α-bromo-17-hydroxy-compounds to be isolated from the reduction of the (stable) 16β-bromo-ketones is based on a mistaken assumption as to the position of the equilibrium

between the two stereoisomeric bromo-ketones (see also below), and disregards the practical difficulty of isolating minor products from such mixtures.

Conclusion (ii) by Shoppee, Jenkins, and Summers,[3] that the position of equilibrium differs among the three pairs of 16-bromo-17-ketones, is based on a comparison of their findings with our results and involves a misinterpretation of the latter. In no case have we claimed that the epimeric mixtures obtained in our work are equilibrium mixtures; we stated only the compositions resulting under the experimental conditions. We have now equilibrated both epimerides of 16-bromo-5α-androstan-17-one (III) and (IV), and of 3β-acetoxy-16-bromo-5α-androstan-17-one (XII) and (XIII), under the conditions used by Shoppee and his co-workers, *i.e.*, in 4% hydrogen bromide in glacial acetic acid at 55°, the progress of the reaction being followed polarimetrically. The course of the reaction was the same analogous for both the 16α-bromo-ketones, and the final rotation corresponded to a mixture containing 73 ± 2% of the β-epimeride. Equilibration of both the 16β-bromo-ketones also took the same course, the final rotation values indicating 67 ± 2% of the 16β-bromo-derivative. The average equilibrium compositions, about 70% of the β-epimeride, are significantly different from the result recorded by Shoppee, Jenkins, and Summers (β 53 ± 3%, α 47 ± 3%), but reasonably close to the composition reached by alkaline equilibration (β about 75%; α 25%).*

Any differences in the conformation of ring D sufficient to affect the chemical behaviour of substituents in positions 16 or 17 would be expected to be reflected in the infrared spectra of the 16-bromo-17-alcohols. Nickon's findings[6] and our work on steroid bromohydrins[7] show that the O–H stretching frequency of these compounds depends on the steric relation of the bromo- and hydroxy-substituents in a regular and sensitive way. We have confirmed the preparations and determinations of configuration of the four 16-bromo-5α-androstan-17-ols (V, VI, and VII; R = H) and (X) described by Shoppee, Jenkins, and Summers[3] [a minor difference was that lithium aluminium hydride reduction of the bromo-ketone (III) in our hands gave both the 17β- and 17α-hydroxy-isomers, in agreement with our earlier results[1,2] in the 3-substituted series; both the acetates (VI and VII; R = Ac) were isolated by crystallisation after acetylation of the crude product]. The frequencies of the O–H stretching vibrations for the four 16-bromo-5α-androstan-17-ols are recorded in the Table, with similar data for a number of other,

5α-Androstane derivative	$\nu_{max.}$ (cm.$^{-1}$) (in CCl_4)	$\Delta\nu$ [a] (cm.$^{-1}$)
17β-Ol	3624	
3β-Acetoxy-17β-ol	3624	
16α-Bromo-17β-ol	3619	5
16α-Bromo-3β-methoxy-17β-ol	3617	7
16β-Bromo-17β-ol	3554	71
3β-Acetoxy-16β-bromo-17β-ol	3550	74
16β-Bromo-3β-methoxy-17β-ol	3552	72
17α-Ol	3626	
3β-Acetoxy-17α-ol	3625	
16β-Bromo-17α-ol	3618	8
16α-Bromo-17α-ol	3558	68
16α-Bromo-3β,17α-diol	3558, 3618 [b]	69

[a] Frequency shift referred to the 16-unsubstituted compounds. [b] 3-OH group.

3β-substituted compounds of the same type. No significant difference can be detected betweeen the 3-unsubstituted and the corresponding 3β-oxygenated compounds of the same type. Even the introduction of a double bond in position 5,6 causes no appreciable deviation (see ref. 7). The only infrared frequency recorded by Shoppee and his co-workers[3] for this group is that for the O–H vibration in 16α-bromo-5α-androstan-17β-ol

* The equilibrium mixture obtained by acid treatment of 16α-bromo-œstrone acetate is reported[5] to contain " predominantly " the 16β-epimeride.

[5] Fishman and Biggerstaff, *J. Org. Chem.*, 1958, **23**, 1190.
[6] Nickon, *J. Amer. Chem. Soc.*, 1957, **79**, 243.
[7] Horák and Fajkoš, *Coll. Czech. Chem. Comm.*, 1959, **24**, 1515.

(VI; R = H), which is given as 3632 cm.$^{-1}$, a shift of +8 cm.$^{-1}$ from that for the unsubstituted androstan-17β-ol. However, in Nickon's work and in our own substitution by bromine invariably caused a negative shift, as, indeed, do all other forms of hydrogen-bonding from their very nature. We therefore regard this value as erroneous. (In all other respects the infrared and rotational values recorded and discussed by Shoppee, Jenkins, and Summers [3] are substantially in accord with our earlier findings and discussion.[1,2])

Discrepancy (iii) referred to by Shoppee, Jenkins, and Summers [3]—conversion of 16α-bromo-5α-androstan-17β-ol (VI; R = H) into 5α-androstan-17-one (I) by alkali—is contrary to all experience in this field, whereby a *trans*-bromohydrin of this type is invariably converted into the epoxide. Indeed, from the 16α-bromo-17β-alcohol (VI; R = H) and methanolic potassium hydroxide under conditions used by Shoppee *et al.* we obtained a practically quantitative yield of 16β,17β-epoxy-5α-androstane (VIII); no infrared carbonyl absorption could be detected even in the crude product. The constitution of the epoxide was confirmed by independent synthesis from the 16α,17α-epoxide [3] (IX) through the diol monoacetate (XI; R = H) and its methanesulphonate (XI; R = Me·SO_2), the infrared spectra of the two products being identical. We cannot account for this difference in experimental findings.

Experimental

M. p.s were measured on a Kofler block. Samples for analysis were dried at 90°/0·002 mm. for 8 hr. Unless otherwise stated, $[\alpha]_D$ is for $CHCl_3$ solutions at 20°. Infrared spectra were measured for CCl_4 solutions on a Zeiss-Jena UR 10 double-beam spectrometer with lithium fluoride optics.

17-*Acetoxy*-5α-*androst*-16-*ene* (II).—5α-Androstan-17-one (10·75 g.), dried azeotropically with benzene, in isopropenyl acetate (70 c.c.) was treated with concentrated sulphuric acid (0·05 c.c.), and 30 c.c. of the mixture were distilled off during 2 hr. More isopropenyl acetate (70 c.c.) and sulphuric acid (0·05 c.c.) was then added and 70 c.c. were distilled off during 2 hr. The mixture was diluted with light petroleum (b. p. 40—60°; 1500 c.c.), filtered through alkaline aluminium oxide (activity I; 50 g.), and evaporated to dryness, and the residue crystallised from methanol to give 17-*acetoxy*-5α-*androst*-16-*ene* (8·0 g., 65%), m. p. 84—85°, $[\alpha]_D$ +36·5° (*c* 3·2) (Found: C, 79·6; H, 10·2. $C_{21}H_{32}O_2$ requires C, 79·7; H, 10·2%).

16α-*Bromo*-5α-*androstan*-17-*one* (III).—A solution of 17-acetoxy-5α-androst-16-ene (8·0 g.) in carbon tetrachloride (200 c.c.) was treated in 15 min. at 0°, with stirring, with bromine (4·1 g.) in carbon tetrachloride (50 c.c.). The mixture was washed with sodium thiosulphate solution, sodium hydrogen carbonate solution, and water, dried, and evaporated. The residue on repeated crystallisation from ethanol yielded 16α-bromo-5α-androstan-17-one (7·7 g., 87%), m. p. 196—197°, $[\alpha]_D$ +58° (*c* 2·4); Shoppee *et al.*[3] record m. p. 197°, $[\alpha]_D$ +58°.

Reduction of 16α-*Bromo*-5α-*androstan*-17-*one* (III) *with Sodium Borohydride*.—(*a*) A solution of 16α-bromo-5α-androstan-17-one (2·0 g.) in absolute ethanol (350 c.c.) was treated, at 0°, with sodium borohydride (580 mg.) and set aside at +4° for 15 hr. The mixture was worked up in the customary manner and the crystalline residue recrystallised from methanol to give 16β-bromo-5α-androstan-17β-ol (1·28 g., 64%), m. p. 122—123°, $[\alpha]_D$ +2° (*c* 2·7), $\nu_{max.}$ 3554 cm.$^{-1}$ (O–H stretching); Shoppee *et al.*[3] record m. p. 123°, $[\alpha]_D$ +3·5°. Treatment with acetic anhydride in pyridine afforded the *acetate* (V; R = Ac), m. p. 144°, $[\alpha]_D$ +61° (*c* 1·2) (Found: C, 63·3; H, 8·2; Br, 19·8. $C_{21}H_{33}O_2Br$ requires C, 63·5; H, 8·4; Br, 20·1%).

(*b*) The 16α-bromo-17-ketone (340 mg.) was reduced as under (*a*), and the crude product chromatographed on neutral aluminium oxide (activity III—IV; 30 g.) from light petroleum (b. p. 40—60°)–benzene (1 : 1), 30 c.c. fractions being taken. Fractions 2—6 afforded the 16β-bromo-17β-alcohol (233 mg.), fractions 9—13 androstan-17β-ol (80 mg.), m. p. and mixed m. p. 164—165°, $[\alpha]_D$ +13° (*c* 1·6).

(*c*) The 16α-bromo-17-ketone (340 mg.) in ether (25 c.c.) was treated with sodium borohydride (100 mg.) in methanol (12 c.c.) at 20° for 18 hr. as described by Shoppee *et al.*,[3] and worked up in the same manner, affording 16α-bromo-5α-androstan-17α-ol (215 mg.), m. p. 127—129° (from methanol), $[\alpha]_D$ −4° (*c* 1·3), $\nu_{max.}$ 3558 cm.$^{-1}$ (O–H stretching) {acetate, m. p. 206—207° (from methanol), $[\alpha]_D$ −5° (*c* 1·3)}, and 16α-bromo-5α-androstan-17β-ol (79 mg.), m. p.

XUM

93—95° (from methanol), $[\alpha]_D$ +2° (*c* 1·4), $\nu_{max.}$ 3619 cm.$^{-1}$ (O–H) stretching) {acetate, m. p. 144—145°, $[\alpha]_D$ −30° (*c* 1·2)}. Shoppee *et al.*[3] record, for an analogous experiment: 17α- (140 mg.), m. p. 125—126°, $[\alpha]_D$ −5° {acetate, m. p. 200—203°, $[\alpha]_D$ −5°}; 17β- (130 mg.), m. p. 90—94°, $[\alpha]_D$ +3°, $\nu_{max.}$ 3632 cm.$^{-1}$ (O–H stretching) {acetate, m. p. 142—144°, $[\alpha]_D$ −31°}.

Reduction of 16α-*Bromo-5α-androstan-17-one* (III) *with Lithium Aluminium Hydride.*—16α-Bromo-5α-androstan-17-one (830 mg.) in dry ether (150 c.c.) was treated at 0° with lithium aluminium hydride (400 mg.), and the mixture was set aside at 0° for 3½ hr., then worked up in the customary manner. The crude product was treated with acetic anhydride in pyridine, and the acetyl derivatives were fractionally crystallised from ethanol and ethyl acetate, to yield 17β-acetoxy-16α-bromo-5α-androstane (510 mg.), m. p. 143—145°, $[\alpha]_D$ −32° (*c* 1·8), together with the 17α-epimer (120 mg.), m. p. 203—206°, $[\alpha]_D$ −4° (*c* 1·9).

16β-*Acetoxy-5α-androstan*-17α-*ol* (XI; R = H).—16α,17α-Epoxyandrostane[3] (805 mg.) in acetic acid (12 c.c.) was heated to 100° under nitrogen for 2½ hr., the mixture diluted with water and worked up in the customary manner, and the crude product chromatographed on aluminium oxide (30 g.) from light petroleum (b. p. 40—50°)–benzene (2 : 1). Elution with benzene–ether (1 : 1) gave 248 mg. of crystals which on recrystallisation from methanol afforded 16β-*acetoxy-5α-androstan*-17α-*ol* (205 mg.), m. p. 174—175°, $[\alpha]_D$ −14° (*c* 2·08) (Found: C, 75·2; H, 10·2. $C_{21}H_{34}O_3$ requires C, 75·4; H, 10·3%).

This product (150 mg.) with methanesulphonyl chloride (0·25 c.c.) in pyridine (2 c.c.) at 0° (2½ hr.) gave the *methanesulphonate* (150 mg.), m. p. 146—147° (from methanol), $[\alpha]_D$ 0° (Found: C, 63·9; H, 8·7; S, 7·5. $C_{22}H_{36}O_5S$ requires C, 64·0; H, 8·8; S, 7·8%).

16β,17β-*Epoxy-5α-androstane* (VIII).—(*a*) The foregoing methanesulphonate (150 mg.) in ether (4 c.c.) was refluxed with potassium hydroxide (150 mg.) in methanol (15 c.c.) for 1 hr., giving, after crystallisation from methanol, 16β,17β-*epoxy-5α-androstane* (87 mg.), m. p. 113—114°, $[\alpha]_D$ +40·2° (*c* 1·4) (Found: C, 83·1; H, 10·9. $C_{19}H_{30}O$ requires C, 83·2; H, 11·0%).

(*b*) 16α-Bromo-5α-androstan-17β-ol (270 mg.) was refluxed with potassium hydroxide (270 mg.) in methanol (28 c.c.) for 8 hr. and worked up in the usual manner. The crystalline residue, m. p. 112—114°, showed no infrared carbonyl absorption and contained no halogen. Crystallisation from methanol afforded 16β,17β-epoxy-5α-androstane (165 mg.), m. p. and mixed m. p. 114°, $[\alpha]_D$ +39·3° (*c* 1·7) (Found: C, 83·1; H, 10·8%).

Equilibration of the 16-*Bromo*-17-*ketones* (III, IV, XII, *and* XIII) *in Acid Solution.*—(*a*) 16α-Bromo-5α-androstan-17-one (155 mg.; $[\alpha]_D$ +58°) in acetic acid (9 c.c.) was treated with a 40% solution (1 c.c.) of hydrogen bromide in acetic acid and kept at 55°, the optical rotation being measured at hourly intervals. After 4 hr., $[\alpha]_D$ became constant at +106°, corresponding to 73 ± 2% of the β-epimeride in the mixture. {All calculations of composition are based on rotation values for the pure epimerides obtained in glacial acetic acid; these were identical with the values obtained in chloroform except for (XIII), which had $[\alpha]_D$ +97° (*c* 1·13) in acetic acid.} By the usual working-up the mixture gave a product of $[\alpha]_D$ +104° (70 ± 2% of β-epimeride) which on crystallisation from ethanol afforded 16β-bromo-5α-androstan-17-one (58 mg.), m. p. 126—127°, $[\alpha]_D$ +125°.

(*b*) 3β-Acetoxy-16α-bromo-5α-androstan-17-one (320 mg.) under the conditions described above gave a mixture of $[\alpha]_D$ +80° (71 ± 2% of β-epimeride); the crude crystalline product, $[\alpha]_D$ +79° (70 ± 2% of β-epimeride), on crystallisation from methanol gave 3β-acetoxy-16β-bromo-5α-androstan-17-one (125 mg.), m. p. 147°, $[\alpha]_D$ +94°.

(*c*) Under the same conditions, 16β-bromo-5α-androstan-17-one gave a final mixture of $[\alpha]_D$ +102° (67 ± 2% of β-epimeride); 3β-acetoxy-16β-bromo-5α-androstan-17-one gave a mixture of $[\alpha]_D$ +76° (65 ± 2% of β-epimeride).

Epimerisation of the 16α-*Bromo*-17-*ketones* (III) *and* (XII) *in Alkaline Solution.*—(*a*) Sodium borohydride (50 mg.) in ethanol (10 c.c.) was treated with acetone (0·5 c.c.) and, after 2 hr. at 15°, 16α-bromo-5α-androstan-17-one (200 mg.) in ethanol (5 c.c.) was added. Two minutes after mixing, $[\alpha]_D$ of the solution was +108°, corresponding to 76 ± 2% of the β-epimeride. The crude product (190 mg.), m. p. 110—120°, isolated in the usual way, had $[\alpha]_D$ +111° (80 ± 2% of β-epimeride) (Found: Br, 22·7%). Crystallisation from ethanol afforded pure 16β-bromo-5α-androstan-17-one (105 mg.), m. p. 127°, $[\alpha]_D$ +124°. In an analogous experiment, 3β-acetoxy-16α-bromo-5α-androstan-17-one gave an equilibrated solution of $[\alpha]_D$ +83° (77 ± 2% of β-epimeride) and, after working up, a crude product, m. p. 102—125°, $[\alpha]_D$ +85° (80 ± 2% of β-epimeride) (Found: Br, 19·5%). Crystallisation from ethanol afforded pure 3β-acetoxy-16β-bromo-5α-androstan-17-one, m. p. 146°, $[\alpha]_D$ +95°.

(*b*) To a 0·2% methanolic solution of sodium hydroxide (7 c.c.), the bromo-ketone (III) (100 mg.) in chloroform (1 c.c.) was added. After 20 min. at 15°, when the rotation of the solution was +105° (71 ± 2% of β-epimeride), the mixture was worked up in the usual way, to give a crude product, m. p. 110—125°, $[\alpha]_D$ +103° (68 ± 2% of β-epimeride) (Found: Br, 22·6%). The bromo-ketone (XII) in the same way gave a solution of $[\alpha]_D$ +79° (70 ± 2% of β-epimeride) and a crude product, m. p. 98—116°, $[\alpha]_D$ +79° (Found: Br, 19·1%). The pure β-bromo-ketones (IV) and (XIII) were again isolated by crystallisation of the crude products from ethanol. Closely similar results were obtained with ethanol as the solvent in the equilibration.

The author thanks Academician F. Šorm for his continued and active interest in this work.

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799. *An Infrared Study of the Methylhydroxylamines.*

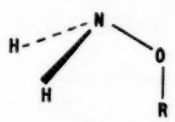
By MANSEL DAVIES and N. A. SPIERS.

The five methyl derivatives of hydroxylamine have been prepared, and their infrared spectra recorded between 4000 and 420 cm.$^{-1}$. All were studied in the gaseous state and as liquid or in carbon tetrachloride solution.

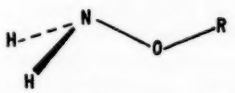
From a study of the contours of the vapour absorptions, deductions as to the molecular conformations are possible. The data indicate that the nitrogen valencies are pyramidally inclined and that a skew or *trans*-conformation about the N–O axis is preferred. For the *O*-methyl and *NN*-dimethyl derivatives, and also possibly in *N*-methylhydroxylamine, there is suggestive evidence of two structures' being present in the vapour.

The C–N, N–O, and C–O bond stretching frequencies observed as combined modes for the skeletal vibrations are such as to establish the simple single bonds consonant with the sp^3 hybridized states of the C and N atoms. The methyl group frequencies show striking constancy and simplicity in these compounds.

APART from a study of *O*-methylhydroxylamine in the photographic region,[1] no infrared study of the methylhydroxylamines has been reported: neither are there Raman spectra available. These omissions were almost certainly due to the absence of adequately detailed accounts of the preparation and properties of some of the five methyl derivatives of hydroxylamine. Only after much of the present preparative work was complete were we helped by the appearance of satisfactory details for some of them.[2] Our aim was to report the spectra in the region 2—25 μ for the five methylhydroxylamines: to inter-



(I)



(II)

relate and, as far as possible, assign the frequencies to component molecular vibrations: to deduce the probable molecular configurations of these derivatives; and to assess intermolecular interactions in the liquid or the solution state by comparison of the absorption spectra with those of the vapours. Few simple molecules with adjacent single C–O, C–N, and N–O bonds have been studied by infrared methods, although much attention has

[1] Thompson, *J. Chem. Phys.*, 1939, **7**, 442.
[2] Bissot, Parry, and Campbell, *J. Amer. Chem. Soc.*, 1957, **79**, 796.

XUM

been given to the amides and their derivatives in which many complications in relation to molecular vibrational frequencies occur.

The parent compound, hydroxylamine, has been the subject of infrared studies in the vapour and the solid state.[3] A feature of the vapour study was the suggestion of the existence of two isomers, "*cis*" (I; R = H) and "*trans*" (II; R = H) forms with the possibility of the latter's being, in the vapour, the more stable, although the *X*-ray crystallographic evidence shows the *trans*-conformation in the solid state.[4] Even for the simplest methylhydroxylamine a spectrometer capable of no better resolution than 1 cm.$^{-1}$ (the operating limit for our instrument) will provide only band envelopes for the vapour absorptions. For asymmetric top molecules, such as are all the methylhydroxylamines, Badger and Zumwalt[5] have calculated the contours of band envelopes associated with vibrations in which the dipole-moment change is parallel to the axis of least (A), median (B), or greatest (C) moment of inertia. This they have done in terms of two parameters s and ρ which are simple functions of I_A, I_B, and I_C.

In using Badger and Zumwalt's curves as indications of what the ideal *A*, *B*, and *C* type vibrational band-contours would be, we have calculated by Hirschfelder's procedure[6] the moments of inertia for alternative plausible configurations of the methylhydroxylamine structures. Normal bond lengths and angles have been assumed in these calculations: *e.g.*, bond lengths in Å: C–H = 1·09; O–H = 0·96; N–H = 1·01; N–O = 1·46; C–O = 1·43; C–N = 1·47: bond angles, HCH = 109°; HNH = 107°; NOH = 103°; ONH = 105°; CNO = 105°; CNH = 107°, etc. The actual directions of the axes in the assumed structures are readily found by successive trials. In addition to the form of the contours, a check in identification is also possible from the predicted separation of the component features. Two uncertainties must be faced. First, the direction of the dipole-moment change in a particular vibration can only be approximately fixed for the simplest vibrational forms, *e.g.*, ν(C–O), ν(O–H), $\nu_{sym}(CH_3)$, $\nu_{sym}(NH_2)$ $\nu_{as}(NH_2)$, d(O–H), $d(NH_2)$, etc.; but this

(III) (IV) (V)

can be done with adequate qualitative correctness, provided the influence of hybridization changes of the "lone pair" electrons on the nitrogen due to orbital-following in the NH_2 vibrations, are allowed for. Secondly, only a minority of such vibrations will have dipole changes close to one of the principal axes: the majority will be of a mixed character. Accordingly, only a probability status attends structural deductions based on the identification of the contours.

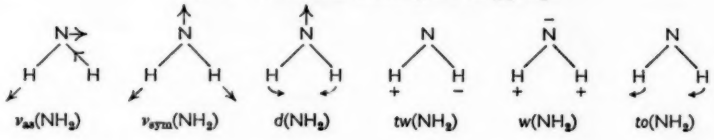
A significant representation of the conformation around the O–N bond in the hydroxylamines is obtained by projecting the structure as seen by looking along the O–N line, if we remember that the "lone-pair" electrons will complete a trigonal pattern about the O and N centres. In this respect it is relevant to recall the skew conformation of the "iso-electronic" molecules hydrogen peroxide (III), hydroxylamine (IV), and hydrazine (V).[7]

[3] Giguère and Lin, *Canad. J. Chem.*, 1952, **30**, 948.
[4] Meyers and Lipscomb, *Acta Cryst.*, 1955, **8**, 583.
[5] Badger and Zumwalt, *J. Chem. Phys.*, 1938, **6**, 712.
[6] J. O. Hirschfelder, *J. Chem. Phys.*, 1940, **8**, 431.
[7] (*a*) See "Tables of Interatomic Distances, etc.," Chem. Soc. Special Publ. No. 11, 1958; (*b*) Penney and Sutherland, *Trans. Faraday Soc.*, 1934, **30**, 898; *J. Chem. Phys.*, 1934, **2**, 492.

For such an angular grouping as NH_2 a variety of vibrational modes is involved within a polyatomic structure. For the plane of the equilibrium positions of the atoms the displacements can be represented as in Fig. 1, where, in the probable order of decreasing frequencies we have the antisymmetric $\nu_{as}(NH_2)$ and symmetric $\nu_{sym}(NH_2)$ stretching modes; the in-plane deformation $d(NH_2)$; the twisting, $tw(NH_2)$; the wagging, $w(NH_2)$; and the torsional $to(NH_2)$.

For the CH_3 group corresponding modes are often of values *ca.*: $\nu_{as}(CH_3) = 2960$ cm.$^{-1}$; $\nu_{sym}(CH_3) = 2870$ cm.$^{-1}$; $d_{as}(CH_3) = 1450$ cm.$^{-1}$; $d_{sym}(CH_3) = 1380$ cm.$^{-1}$; rocking and wagging of the H_3 group in CH_3, the former by convention being the motion in the plane

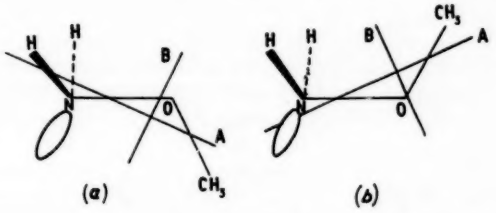
FIG. 1. *Vibrational modes of the* NH_2 *group.*



of the skeleton; the wagging motions perpendicular to that plane are within the range 800—1200 cm.$^{-1}$; the torsional mode $to(CH_3)$ *ca.* 300 cm.$^{-1}$. It is the external group vibrational modes (twisting, rocking or wagging, torsional) which are particularly sensitive to the mechanical coupling and bonding between the group and the remainder of the molecule.

O-*Methylhydroxylamine.*—The extreme "*cis*" and "*trans*" conformations for this molecule are represented in Fig. 2, with the positions of the corresponding principal axes and of the so-called "atomic" or better "orbital" moment of the lone-pair electrons: the C-axis is perpendicular to the A,B plane.[7a] These conformations are, respectively, the staggered "*cis*" and eclipsed "*trans*" form: other special orientations around the N–O bond are the eclipsed "*cis*" and staggered "*trans*" forms. For both forms in Fig. 2, in units of 10^{-40} g. cm.^{2}, the moments of inertia are $I_A = 31 \pm 2$, $I_B = 92 \pm 2$,

FIG. 2. *Principal axes for the* trans (a) *and* cis (b) *conformations of* O-*methylhydroxylamine. (The* C *axis is at right angles to the plane of the diagram.)*



$I_C = 113 \pm 2$. These values predict a separation of the component features in the band contours of *ca.* 15 cm.$^{-1}$, *i.e.*, *A* and *C* types will be of total width 30 cm.$^{-1}$; whilst the doublet spacing in *B*-type absorptions should be near 15 cm.$^{-1}$.

A total of 18 proper modes can be expected for this molecule. Plausible descriptions for 15 of these have already been given, *i.e.*, six modes arising from the NH_2 group and nine from the CH_3 group, as for the latter the antisymmetric stretching and deformation modes are doubly degenerate. The three remaining vibrations are the "skeletal modes" of the N–O–C group, *i.e.*, $\nu_{as}(NOC)$, $\nu_{sym}(NOC)$, and $d(NOC)$.

The observations are summarized in Table 1. No Raman spectrum is available. Many of the suggested assignments follow from the normal group frequencies and, in particular, there is good correlation with those in "*O*-methylformhydroxamic acid,"[8] H·CO·NH·O·CH_3, which is the formyl derivative of *O*-methylhydroxylamine.

[8] Parsons, *J. Mol. Spectroscopy*, 1958, **2**, 566.

The stretching NH_2 modes are of particular interest (Fig. 3). In the vapour $\nu_{as}(NH_2)$ appeared as an unsymmetrical contour with a sharp centre at 3414 cm.$^{-1}$ having wings at

TABLE 1. *Infrared absorption frequencies (cm.$^{-1}$) in O-methylhydroxylamine.*

Liquid	Soln. in CCl_4	Vapour		Assignment	Liquid	Vapour		Assignment
3539(sh)					1876vw			
3377(sh)						1600		
		3429				1592	s	
3308vs	3326ms	3414	vw	$\nu_{as}(NH_2)$	1593s	1588		$d(NH_2)$
		3406				1573		
3294(sh)		3289			1464s	1475m		$d_{as}(CH_3)$
		3278			1438s	1439m		$d_{sym}(CH_3)$
3240s	3244ms	3269	vw	$\nu_{sym}(NH_2)$	1316ms	1310vw		$\nu_{sym}(NOC) + d(NOC)$?
		3256			1212m	1211s		wag.(CH_3)
		3203				1185		
		3191			1168ms	1174	vs	
3157s		3181	vw	$2d(NH_2)$		1152		
		3168			1143ms	1124m		rock.(CH_3)
2979s	2982s	2987s				1015		
2938vs	2938vs	2950vs		$\nu_{as}(CH_3)$	1012ms	998	vs	$\nu_{as}(NOC)$
2895vs	2890vs	2900vs		$2d_{as}(CH_3)$		987		
2811vs	2812ms	2817ms		$\nu_{sym}(CH_3)$	846s	858vw		$\nu_{sym}(NOC)$
					450m	487w		$d(NOC)$

3406 cm.$^{-1}$ and 3429 cm.$^{-1}$. It can only be described as a hybrid form with certainly some *C*-component. Neither is the $\nu_{sym}(NH_2)$ absorption of simple form: it has two central peaks at 3269 and 3278 cm.$^{-1}$ flanked by shoulders at 3256 and 3289 cm.$^{-1}$. This might

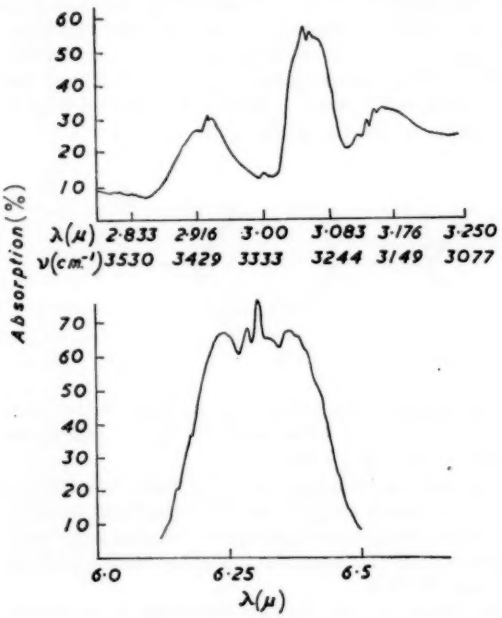


FIG. 3. *The $d(NH_2)$ and $\nu(NH_2)$ bands in O-methylhydroxylamine vapour (traced from the actual records).*

be taken as a *C*- or hybrid *AC*-type absorption but for the second marked central peak at 3278 cm.$^{-1}$. These observations suffice to rule out the " eclipsed *trans* " conformation of Fig. 2, since for that it is expected that $\nu_{as}(NH)_2$ would be a pure *C*-type and $\nu_{sym}(NH_2)$ a pure *B*-type absorption. The alternatives appear to be an " eclipsed *cis* " or a " staggered

trans" form. The considerations presuppose the absence of completely free rotation around the N–O bond, but as such freedom is not present in either hydrogen peroxide or hydrazine it is unlikely to be present in *O*-methylhydroxylamine.

The deformation $d(NH_2)$ mode provides further criteria (Fig. 3). Its absorption is certainly that near 1600 cm.$^{-1}$ which, in the vapour, has a distinct *C*-type character with a with a well-defined *Q* branch at 1588 and wings at 1603 and 1573 cm.$^{-1}$. This form leads to the same alternatives as the stretching frequencies but again there is an additional sharp peak, at 1592 cm.$^{-1}$. Being on the high-frequency side of the principal *Q*-branch it is perhaps unlikely that this is a "hot band" associated with the same mode, but it could be a subsidiary absorption (overtone or combination) with an unusually sharp centre. Nevertheless, to rate it no higher, the possibility remains that this second central feature, like that at 3278 cm.$^{-1}$ in $\nu_{sym}(NH_2)$, arises from the presence of two species of molecule having slightly different conformational forms, *e.g.*, that both "eclipsed *cis*" and "staggered *trans*" forms occur. It is significant that a similar state of affairs has been suggested in hydroxylamine itself.

Again, with sufficient vapour in the cell to bring up the NH_2 stretching modes, a distinct absorption appears from 3140 to 3200 cm.$^{-1}$ which is too broad to come from a single vibration. The most plausible assignment of this is as an overtone of the relatively intense $d(NH_2)$ absorption, *i.e.*, 2×1588 cm.$^{-1}$, and the existence of component peaks near 3168, 3181, 3191, and 3203 cm.$^{-1}$ could also be explained by the presence of two molecular species.

The intensities of the $\nu(NH_2)$ absorptions are noteworthy. Although of equal intensity to the $\nu(CH_3)$ modes in the liquid, they are not obvious as vapour absorptions until the cell shows 100% absorption in the $\nu(CH_3)$ region. Contrary to the usual order, but as is found in hydroxylamine itself, the $\nu_{sym}(NH_2)$ is more intense than $\nu_{as}(NH_2)$ in the vapour. An explanation is provided by considering the probable dipole-moment changes during the vibrations, taking particular account of the contributions from the lone-pair electrons—as is also essential in assessing the probable direction of these dipole-moment changes.[9] In carbon tetrachloride solution the sequence of the NH_2 intensities has reverted to normal, although they are still less strong than the $\nu(CH_3)$ absorptions, equality with which they attain in the liquid state. For the latter, the $\nu_{as}(NH_2)$ and $\nu_{sym}(NH_2)$ centres are best located at 3308 and 3157 cm.$^{-1}$ respectively, *i.e.*, at values -106 and -112 cm.$^{-1}$ with respect to the vapour centres. These displacements are a measure of the hydrogen-bridge interaction, most probably (N–H----O) which occurs in the liquid. Adjacent subsidiary maxima (3294 and 3240 cm.$^{-1}$) in the liquid are probably features in the absorption by the hydrogen-bridge structure or (less probably) arise from alternative interactions, *e.g.*, (N----H).

In the region of the CH_3 stretching modes four strong centres are found, in order of decreasing intensities in the liquid at 2938, 2895, 2979, and 2811 cm.$^{-1}$, and at closely similar values in carbon tetrachloride. The assignment of the first and the last of these to $\nu_{as}(CH_3)$ and $\nu_{sym}(CH_3)$ is arrived at by consideration of the alternatives and noting the agreement of these values with those in *O*-methylformhydroxamic acid [8] (2941 and 2828 cm.$^{-1}$) and with the findings of Henbest *et al.*[10] for the methyl group in O–CH_3 structures.

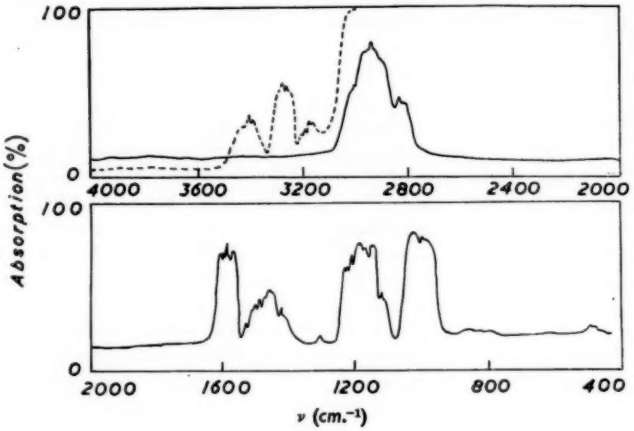
The absorption at 2895 cm.$^{-1}$ (a similarly strong one is found in $CH_3 \cdot NH_2$ and the methyl halides) can be assigned to the overtone of $d_{as}(CH_3)$, *i.e.*, 2×1461 cm.$^{-1}$, intensified by its coincidence with the $\nu(CH_3)$ frequency region. This still leaves 2979 cm.$^{-1}$, and it is impossible to assign this frequency (or 2938 cm.$^{-1}$) either as an overtone or as a binary combination tone. It is difficult to resist the suggestion that it is $\nu_{as}(CH_3)$ in a molecular conformation different from that of the 2938 cm.$^{-1}$ absorption: Pozefsky and Coggeshall [11] have recently given for this mode in O–CH_3 groupings values of 2960—2990 cm.$^{-1}$. The

[9] Parsons, Ogden, and Orville-Thomas, *J.*, 1958, 1047.
[10] Henbest, Meakins, Nicholls, and Wagland, *J.*, 1957, 1462.
[11] Pozefsky and Coggeshall, *Analyt. Chem.*, 1951, **23**, 1611.

vapour absorption is complicated in the $\nu(CH_3)$ region by the overlapping of bands (Fig. 4): one of the features that can be recognized is the central (Q) branch of a C-type band at 2987 cm.$^{-1}$ which is the 2979 cm.$^{-1}$ absorption of the liquid, and this form agrees with the suggested assignment. The 2985 cm.$^{-1}$ (liquid) absorption becomes a featureless shoulder at 2900 cm.$^{-1}$ in the vapour.

The $d(CH_3)$ bands also overlap in the vapour absorption to such an extent as to make deductions from their contours uncertain, but the centres are at 1475 and 1439 cm.$^{-1}$ compared with 1464 and 1438 cm.$^{-1}$ in the liquid: in *O*-methylformhydroxamic acid the corresponding values are 1476 (vap), 1468 (liq): 1439 (vap), 1433 (liq). From both its position and its C-type absorption in the vapour centred at 1211 cm.$^{-1}$ there is little doubt that a methyl wagging mode can be recognized—the one out of the (CON) plane. The in-plane rock(CH_3) is at 1124 cm.$^{-1}$ (vap). In *O*-methylformhydroxamic acid the same modes appear in the vapour at 1209 and 1124 cm.$^{-1}$.

FIG. 4. *Infrared spectrum of* O-*methylhydroxylamine vapour at* 110° *in the region* 4000—400 *cm.*$^{-1}$. (*Broken line = increase in amount of vapour.*)



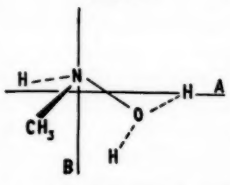
The absorption at 1168 cm.$^{-1}$ (vap), 1174 cm.$^{-1}$ (liq), is an NH_2 mode but it is not clear whether it is the twisting or the wagging vibration: the former is thought the more likely. The essentially A-type absorption at 987–998–1015 cm.$^{-1}$ in the vapour is one of the strongest in the spectrum: it is assigned with confidence to ν_{as}(NOC), which is perhaps very largely the C–O stretching mode. The ν_{sym}(NOC), or N–O stretching mode, is at 858 cm.$^{-1}$ (vap), 846 cm.$^{-1}$ (liq). In hydroxylamine [3] the same mode appears at 895 cm.$^{-1}$ in the vapour, and calculation on a diatomic model shifts this frequency to 825 cm.$^{-1}$ for the *O*-methyl derivative.

For the remaining absorption, a weak vapour band at 487 cm.$^{-1}$ (450 cm.$^{-1}$ liq), there are two possible assignments: deformation (NOC) or torsional (NH_2). The latter occurs at 430 cm.$^{-1}$ in hydroxylamine and is a plausible choice in the present instance: thus d(COC) in dimethyl ether is at 414 cm.$^{-1}$, and the corresponding mode in methylhydroxylamine might be outside the observed range, as is certainly true of the torsional CH_3 mode which we have not found. Another frequency unidentified in the above account is the wagging NH_2. This might be relatively weak and lost amongst the overlapping bands at 1100—1250 cm.$^{-1}$ or under the strong ν_{as}(NOC) at 1000 cm.$^{-1}$.

N-Methylhydroxylamine.—In contrast to the *O*-methylhydroxylamine, which is a volatile liquid (b. p. 48°), this compound is a solid of m. p. 38°, a change which shows the

rôle of hydrogen bridges in the condensed phase. Their influence is also apparent in the differences observed between the liquid and vapour spectra, and as the latter phase shows no signs of such interactions these two sets of observations will suffice for the description of the absorptions.

FIG. 5.



As there is every reason to believe that the nitrogen valencies are pyramidal in hydroxylamine and its *O*-methyl compound, it is reasonable to expect (and observation confirms) that they will be similarly directed in the *N*-methyl compound. This provides configurations of which two extreme versions, the "*cis*" and the "*trans*" form, are represented in Fig. 5. Two of the principal axes will be displaced from the CNO plane by only small amounts, and a number of vibrational modes should be essentially of *A* or *B* character. A differentiation between the above extreme alternatives should be possible on the basis of the OH group absorptions. The absorptions are summarized in Table 2, and the vapour spectrum is shown in Fig. 6.

There is no doubt about the assignment of ν(OH) to the absorption centred at 3646 cm.$^{-1}$ in the vapour which is of an *A* or *AC* type. This suffices to eliminate the "*cis*" form of Fig. 5, as this would give an essentially *B*-type band, a simple doublet of appreciably smaller separation than the observed features. The amount of *C*-character in ν(OH) is of interest, as it would allow one to assess the approach of that hydrogen atom to the "*trans*" position in the CNO plane. As judged by comparison both with the Badger–Zumwalt curves and with an essentially pure *A*-type absorption (1032 cm.$^{-1}$ in vapour) there appears to be a significant *C* component in it. This suggests a skew conformation, and the *d*(OH) vibration, *i.e.*, deformation in the NOH plane, makes this very probable: the absorption has a strong *Q*-branch of distinctly *C*-type (1321 cm.$^{-1}$) which it is difficult to reconcile with the hydrogen in the CNO plane. On the high-frequency side of 1321 cm.$^{-1}$, the pseudo-*P* branch has such abnormally great breadth and intensity (see Fig. 6) that the presence of another absorption is perhaps the only adequate explanation. This must still arise from the *d*(OH) mode, as the whole of this band disappears completely in the liquid state: thus it is possible that a second (*e.g.*, *trans*) azimuthal conformation is present with the skew

TABLE 2. *Infrared absorption frequencies* (*cm.*$^{-1}$) *in* N-*methylhydroxylamine.*

Liquid	Vapour	Assignment	Liquid	Vapour	Assignment
	3656 }			1395vvw	
	3644 } m	ν(OH) monomer		1355 } (sh)	
	3627 }			1333 }	
3550—3000vs		ν(OH) associated		1321 } s	*d*(OH) monomer
	3312w	ν(NH)		1306 }	
3269s		ν(NH)		1207 }	
2978(sh)	2975s		1208m	1196 } m	wag.(CH_3)
2958s	2966vs	$\nu_{as}(CH_3)$		1184 }	
2921(sh)				1140 }	
2891s	2882(sh)		1143w	1126 } w	rock.(CH_3)
2857(sh)				1121 }	
2784m	2791w			1046 }	
1643m			1034vs	1032 } ms	ν_{as}(CNO)
	1518s			1018 }	
	1480		994m	956 } s	ν_{sym}(CNO)
1469m	1462	$d_{as}(CH_3)$		944 }	
1440m	1443	$d_{sym}(CH_3)$		841 }	
	1419		854s	828 } vs	wag.(NH)
1405m		*d*(OH) associated		813 }	
			457m		*d*(CNO)?

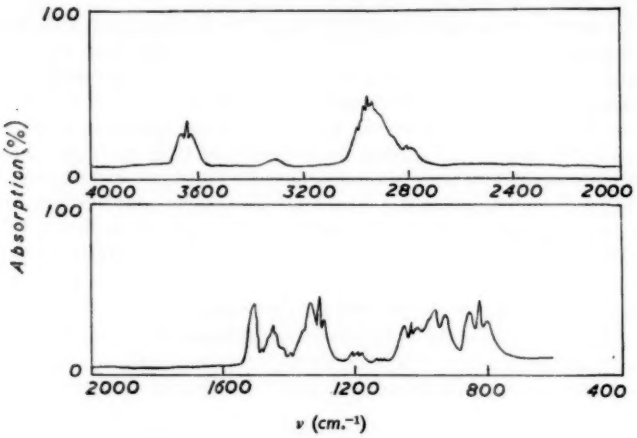
form giving a slightly displaced *d*(OH) frequency. It is not unreasonable to envisage this without its being detectable in any other vibrational absorption in the present study, but the suggestion can be only tentative.

There are seven bonds in the eight-atom molecule giving the stretching vibrations conveniently described as ν(OH), ν(NH), ν_{as}(CNO), ν_{sym}(CNO), $\nu_{sym}(CH_3)$, $\nu_{as}(CH_3)$, the last

being doubly degenerate. The deformation modes should include vibrations based on d(CNO), $d_{sym}(CH_3)$, $d_{as}(CH_3)$ (double), rocking (CH_3), wagging (CH_3), torsional (CH_3): in addition there will be two deformations where the H of NH moves in perpendicular planes (*e.g.*, perhaps in and perpendicular to the HNC plane): similarly for the H of OH where the modes can be described as d(OH) in the HON plane and torsional or to(N–O) in the perpendicular direction.

Considerable hydrogen bonding in the liquid produces a broad absorption in the 3 μ region with a maximum at 3269 cm.$^{-1}$. The latter feature may arise from ν(NH) in the liquid superimposed upon the featureless absorption extending from 3600 cm.$^{-1}$ to below 3000 cm.$^{-1}$, reminiscent of associated OH groups in the alcohols. A weak band seemingly of *B*-type is centred at 3312 cm.$^{-1}$ in the vapour absorptions, and is almost certainly ν(NH) [the mean of the as. and sym. modes in *O*-methylhydroxylamine is 3344 cm.$^{-1}$; and

FIG. 6. *Infrared spectrum of* N-*methylhydroxylamine vapour at* 48° *in the region* 4000—400 *cm.*$^{-1}$.



in the *ON*-dimethyl compound, ν(NH) is at 3283 cm.$^{-1}$]. Its *B*-character is to be expected when the changes in the lone-pair orbital are envisaged.

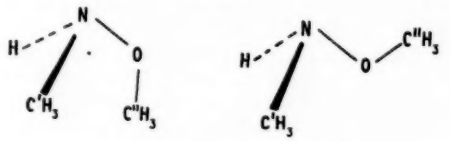
In the liquid spectrum, distinct maxima at 2958, 2891, and 2784 cm.$^{-1}$ are flanked by a number of shoulders. The choice of $\nu_{as}(CH_3)$ as 2958 cm.$^{-1}$ is well supported from related molecules and also 2784 cm.$^{-1}$ for $\nu_{sym}(CH_3)$, as it occurs in the *ON*- and *NN*-di methylhydroxylamines at 2774 and 2776 cm.$^{-1}$, respectively. A feature near 2891 cm^{-1}. also occurs in other methylhydroxylamines and appears to be the overtone $2 \times d_{as}(CH_3)$. In the vapour the overlapping contours provide no clear information.

In the region of the deformation N–H, O–H, and CH_3 modes four absorption maxima appear in the liquid spectrum, at 1643, 1469, 1440, and 1405 cm.$^{-1}$. Those at 1469 and 1440 cm.$^{-1}$ are assigned with some confidence to the $d_{as}(CH_3)$ and $d_{sym}(CH_3)$ vibrations. In the vapour the overlapping features produce a confused contour but a *Q*-branch is located at 1443 cm.$^{-1}$ and shoulders at 1419 and 1462 cm.$^{-1}$. There is no doubt that the strong vapour absorption centred at 1321 cm.$^{-1}$ and already described is the d(OH) mode: in the parent molecule $H_2N{\cdot}OH$ it is at 1357 cm.$^{-1}$; in $H_2C{:}N{\cdot}OH$ at 1315 cm.$^{-1}$; in $(CH_3)_2C{:}N{\cdot}OH$ at 1340 cm.$^{-1}$; and in $(CH_3)_2N{\cdot}OH$ at 1311 cm.$^{-1}$. In the liquid *N*-methylhydroxylamine there are no signs of an absorption from 1250 to 1380 cm.$^{-1}$ and it is the 1405 cm.$^{-1}$ absorption in the liquid which is very probably the principal d(OH) vibration in that phase. Although there is a small shoulder at 1419 cm.$^{-1}$ in the vapour absorption, this is relatively very much weaker than 1405 cm.$^{-1}$ in the liquid. The shift in frequency

from vapour to liquid (+84 cm.$^{-1}$) is characteristic of such deformation modes, especially when the X–H group becomes involved in hydrogen-bonding.

The absorption at 1643 cm.$^{-1}$ is not observed in the vapour. As it occurs in the region of d(NH) modes for secondary amines [12] and appears to have its counterpart at 1592 cm.$^{-1}$ in liquid *ON*-dimethylhydroxylamine it is assigned to d(NH). In the vapour a very strong absorption does appear at 1518 cm.$^{-1}$ with no definite contour. So striking is its disappearance in the liquid that the possibility was considered that it arose from some decomposition in the vapour, but although minor changes could be observed in the vapour spectrum after more than 3 hr. in the heated (55°) cell, the 1518 cm.$^{-1}$ band was prominent in all the records. It is assigned to d(NH) in the vapour and it is noticeable that the liquid has a considerable absorption shoulder from 1500—1600 cm.$^{-1}$ as well as the smaller isolated centre at 1643 cm.$^{-1}$. The latter may well arise from the deformation mode for hydrogen-bonded NH groups, whilst the broad shoulder is the same mode for the unbonded NH groups in the liquid. On this basis both d(OH) and d(NH) show greater integrated intensities in the vapour than in the liquid state, a reversal of the intensity changes in ν(OH) and ν(NH) between the two phases. This pattern of behaviour could well be correlated with the propositions (i) that the X–H bonds acquire greater polar character on being extended in the hydrogen bridge (and hence the stretching modes become more intense and displaced to lower frequencies); (ii) that the hybridization changes in the lone-pair electrons are far greater in the deformation than in the stretching modes; (iii) that such changes are the principal components in the dipole elements involved in the deformation intensities; and (iv) that they are reduced by the smaller amplitudes and higher frequencies of the deformation modes in the hydrogen-bridge systems.

FIG. 7.



"cis" *"trans"*

The rocking CH_3 frequencies are assigned to 1196 cm.$^{-1}$ (vap) ⟶ 1208 cm.$^{-1}$ (liq); 1126 cm.$^{-1}$ (vap) ⟶ 1143 cm.$^{-1}$ (liq), the former probably being that out of the CNO plane although it appears to lack the *C*-character expected of such a mode. The C–N and N–O bonds will have stretching frequencies of the same order and so will combine to give ν_{as}(CNO) and ν_{sym}(CNO) of the triatomic system. These are recognised with some confidence from the distinctively *A*- and *B*-type absorptions in the vapour centred at 1032 cm.$^{-1}$ and 950 cm.$^{-1}$, respectively (cf. 998 cm.$^{-1}$ and 858 cm.$^{-1}$, respectively, in $H_2N{\cdot}O{\cdot}CH_3$). The second deformation mode of NH, perhaps essentially in the HNO plane and describable as a wagging mode, is identified with the *A*- or *AC*-type vapour absorption at 828 cm.$^{-1}$ which, as expected, increases in frequency (to 854 cm.$^{-1}$) in the liquid. The only other absorption found was for the liquid at 457 cm.$^{-1}$. Two of the remaining three proper modes might occur here: the skeletal deformation d(CNO) or the OH torsional or *to*(NO) mode. No good grounds for a choice between these can be advanced although it is reasonably certain that d(CNO) will occur near this frequency; the torsional CH_3 mode is again outside the potassium bromide prism range.

ON-*Dimethylhydroxylamine.*—This compound, b. p. 42°, was examined as a liquid and vapour. The absence of a hydroxyl group reduces the hydrogen-bonding interactions in the liquid to an extent such that the only obvious change in the absorptions on change of phase is a shift of 50 cm.$^{-1}$ in the ν(NH) centre and the breadth of its absorption in the liquid.

[12] Bellamy, "Infra-Red Spectra of Complex Molecules," Methuen, London, 1954.

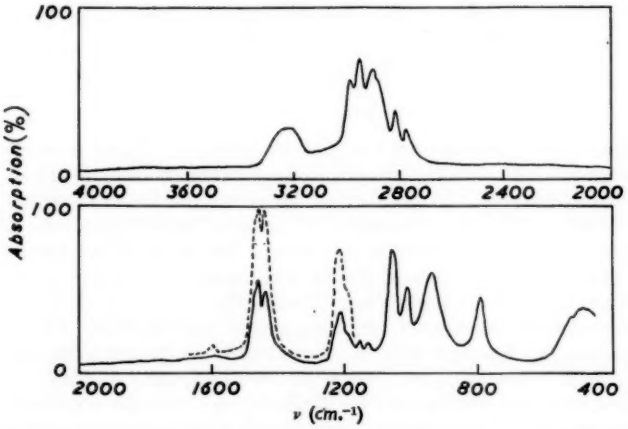
Courtauld models show that the *cis*-conformation of this dimethyl derivative (cf. Fig. 7) would show appreciable congestion of the methyl groups, and something more nearly approaching the *trans*-form is probable.

TABLE 3. *Infrared absorption frequencies (cm.$^{-1}$) in* ON-*dimethylhydroxylamine.*

Liquid	Vapour	Assignment	Liquid	Vapour	Assignment
3234m	3283vw	ν(NH)	1153w	1156w	rock.(CH_3)–O
	3194vw		1133w	1145w	rock.(CH_3)–N
	3135vw	$2d$(NH)		1075	
2977ms	2991(sh)	$\nu_{as}(CH_3)$–N	1057vs	1064 vs	out-of-phase
2939s	2954s	$\nu_{as}(CH_3)$–O		1059	ν(CN) + ν(CO)
2886m	2899s	$2d_{as}(CH_3)$		1032	
2860(sh)			1019m	1022 s	in-phase
2809s	2816s	$\nu_{sym}(CH_3)$–O		1014	ν(CN) + ν(CO)
2775m	2784(sh)	$\nu_{sym}(CH_3)$–N		940	
	1610		928s	933 vs	ν(NO)
1592	1600 w	d(NH)		926	
	1590			813	
1476(sh)			799ms	803 m	wag.(NH)
1460m	1473ms	$d_{as}(CH_3)$		793	
1441m	1434ms	$d_{sym}(CH_3)$	515(sh)		
1219m	1215 s	wag.(CH_3)–O	475	478 m	d(CNOC)?
	1202			457	
1184m		wag.(CH_3)–N			

To the total of 27 vibrational modes, each methyl group will contribute nine. As the likelihood of coupling between the vibrations within these groups is small, any distinction between the nine pairs of frequencies will depend upon whether (CH_3)–O and (CH_3)–N

FIG. 8. *Infrared spectrum of* ON-*dimethylhydroxylamine liquid in the region* 4000—400 *cm.*$^{-1}$. (. . . . = *thicker film.*)



vibrations differ sufficiently. The NH group will contribute one stretching and two bending modes. Three of the remaining six modes will be formed from combinations of the bond stretchings, ν(C'N), ν(NO), ν(C''O); two will be angular deformations d(C''ON), d(C'NO), and finally, a twisting of the skeleton can be described as torsion of the N–O bond. Any attempt to assign a configuration to this molecule on the basis of the band contours is hindered by the fact that it is difficult to attain any certainty as to the form of the skeletal vibrations, because of coupling between the closely similar bond-stretching frequencies.

The observations are summarized in Table 3 and the liquid spectrum is shown in Fig. 8. Most of the assignments are unexceptional. The extreme weakness of ν(NH) in the

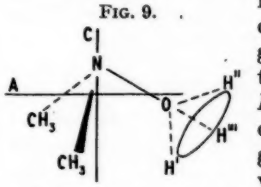
vapour may be noted; it was recorded in an 8 cm. cell at almost atmospheric pressure and was then accompanied by combination tones at 3194 and 3135 cm.$^{-1}$, one of them (3135 cm.$^{-1}$) probably an overtone of the weakly-absorbing deformation mode d(NH) at 1600 cm.$^{-1}$. The *A*-type contour for the latter is one feature providing unequivocal support for a "*trans*"-form of the molecular skeleton.

Whilst a multiplicity of centres both in the liquid- and in the vapour-phase absorptions can be sensibly correlated with the $\nu(CH_3)$–N and $\nu(CH_3)$–O frequencies shown by related molecules in the 3000 cm.$^{-1}$ region, the deformation CH_3 modes show scarcely any signs of differentiation beyond a shoulder at 1476 cm.$^{-1}$ on the main $d_{as}(CH_3)$ centre at 1460 cm.$^{-1}$ (liquid). A group of four absorptions between 1130 and 1220 cm.$^{-1}$ can be plausibly ascribed, two each to the rocking of the (CH_3)–N and (CH_3)–O modes. A further group of strong absorptions between 800 and 1060 cm.$^{-1}$ must contain the three skeletal stretching modes. By comparison with non-planar X_2Y_2 molecules it seems probable that two of these modes may be essentially in-phase and out-of-phase combinations of ν(C′N) and ν(C″O), whilst a third will be a largely symmetrical stretching which could be designated ν(NO). These descriptions can be plausibly given the 1019, 1057, and 928 cm.$^{-1}$ liquid absorptions. The frequencies are in good agreement with expectations from the component bond vibrations in related molecules: thus ν(NO) is at 956 cm.$^{-1}$ in $CH_3{\cdot}NH{\cdot}OH$ and at 858 cm.$^{-1}$ in $H_2N{\cdot}O{\cdot}CH_3$. The remaining absorption in the NaCl region at 799 cm.$^{-1}$ in the liquid, 803 cm.$^{-1}$ in the vapour, is assigned to the wagging NH mode: the only surprising feature is its much greater intensity than the other NH modes.

In the KBr region the liquid shows a broad absorption around 475 cm.$^{-1}$, with a shoulder at 515 cm.$^{-1}$; corresponding features appear, somewhat displaced in frequencies in the vapour. Probably two absorptions are present and it is reasonable to claim, although impossible to establish, that they are both fundamentals: they could be the "in-plane" angular distortion modes of the (CNOC) skeleton. A maximum of 24 out of the 27 fundamentals would thus be accounted for.

NN-*Dimethylhydroxylamine.*—Accepting a pyramidal configuration for the nitrogen valencies, we see that this molecule will be a close approximation to a symmetrical top, the groups attached to the nitrogen atom being CH_3, CH_3, and OH. The one feature open to uncertainty is the orientation of the OH group, and only the ν(OH) and d(OH) modes will be influenced by that. The extreme positions shown in Fig. 9 are "*cis*" and "*trans*" in the plane bisecting the (CNC) angle, which is also the plane of the *A* axis. As it is reasonable to assume for the polar OH group that in ν(OH) the dipole-moment change will be essentially in the O–H direction, this will be largely of *C*, *AC*, or *B* character according as the hydrogen is *cis* (H′), *trans* (H″), or skew (H‴). The deformation mode d(OH), with the hydrogen moving perpendicularly to the O–H line in the NOH plane, will in all cases produce a dipole change closely parallel to the N–O line and so of *AC* character in absorption.

FIG. 9.

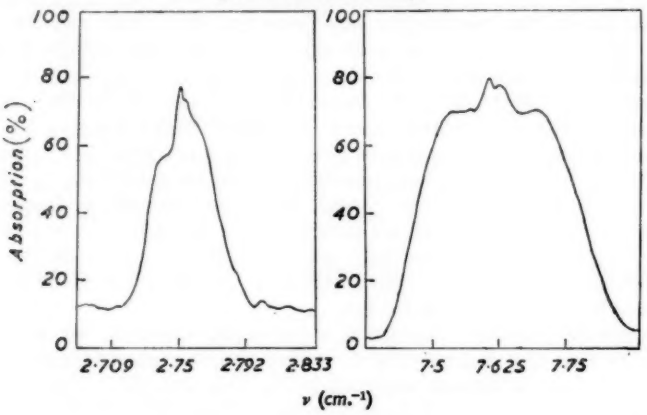


The ν(OH) absorption in the vapour (Fig. 10) reproduces on one side a *C*-type contour, but this is clearly overlaid on the low-frequency side by some further absorption. One suggestion to account for this is the simultaneous presence of two different OH conformations, although it is difficult to specify which. This proposal is strongly supported by the appearance of the d(OH) absorption at 1311 cm.$^{-1}$ in the vapour (Fig. 10). This shows two small central *Q*-branches separated by only 4 cm.$^{-1}$ and each of which might have originated in an *AC*-type absorption. The total width of the strong shoulders of this absorption (1290—1336 cm.$^{-1}$) emphasizes the presence of two overlapping features of essentially similar structure. As only the OH modes show this doubling of *Q*-branches, it is reasonable to associate the features with that group, *i.e.*, with the presence of two angular configurations for the HO group, rather than with the appearance of "hot" bands superimposed on the normal absorptions.

The *NN*-dimethylhydroxylamine, like the *ON*-dimethyl compound, will have 18 fundamental modes associated with the two methyl groups; the hydroxyl group will have its stretching and two bending modes; and the C_2NO skeleton will provide the remaining six. Three of the latter will be stretching modes, and as they will have as their origin three similar bond frequencies each involving the central nitrogen, appreciable coupling between them may be given vibrational forms corresponding to those of the pyramidal molecules (NX_3, etc.).

The observations on the liquid and vapour are briefly summarized in Table 4 and the vapour spectrum is shown in Fig. 11. The hydrogen bonding produces an even larger influence on ν(OH) in the liquid than occurs in *N*-methylhydroxylamine. In the dimethyl compound the shift from the vapour centre in *ca.* 410 cm.$^{-1}$. The strength of the hydrogen bond in these instances is shown by both hydroxyl compounds' having an associated ν(OH)

FIG. 10. *The ν(OH) and d(OH) bands in the vapour spectrum of* NN*-dimethylhydroxylamine (traced from the actual records).*



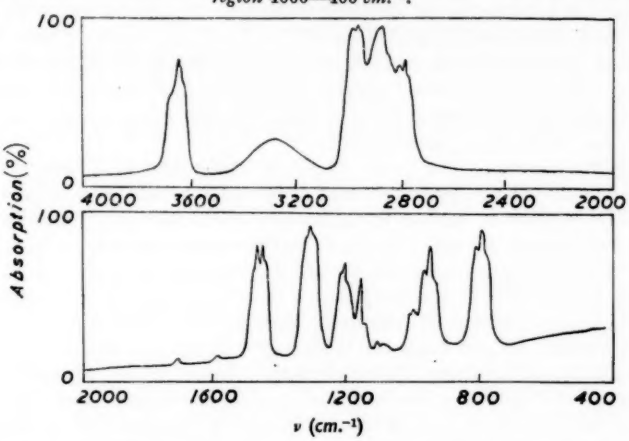
feature in the vapour state which disappears on rise of temperature. In the *N*-methyl compound it is at 3312 cm.$^{-1}$, or 344 cm.$^{-1}$ from the monomer centre; in the dimethyl compound it is at 3271 cm.$^{-1}$, *i.e.*, 365 cm.$^{-1}$ from the monomer centre.

TABLE 4. *Infrared absorption frequencies (cm.$^{-1}$) in* NN*-dimethylhydroxylamine.*

Liquid	Vapour	Assignment	Liquid	Vapour	Assignment
	3651 3636 3631 ms 3621	ν(OH) monomer	1204m	1210 1199 ms 1179	wag.(CH_3)
			1170 1161(sh)		
3600—3000	3400—3200	ν(OH) associated		1154m	rock.(CH_3)
2985(sh)	2966vs	$\nu_{as}(CH_3)$	1090	1089vw	
2946vs		,,	1054w	1069vw	
2865(sh)	2867vs	,,	999m	1000m	skeletal stretching: $\sim\nu_{as}$(CNC)
2857vs		,,			
2821(sh)	2823(sh)	,,		962 950 ms 934	skeletal stretching: ~ν(NO)
2774s	2778s	$\nu_{sym}(CH_3)$	956ms		
	1710vw				
1655m					
	1586vw			803 793 vs 776	skeletal stretching: $\sim\nu_{sym}$(CNC)
1472s	1477s	$d_{as}(CH_3)$	807s		
1439s	1449s	$d_{sym}(CH_3)$			
1419(sh)			501m		skeletal deformation
	1323 1314				
1313vw	1310 vs 1300	d(OH)			

The stretching and deformation modes within the CH_3 groups are assigned in good conformity with the frequencies found from other molecules. Between the extreme centres (2966 and 2778 cm.$^{-1}$) for the $\nu(CH_3)$ frequencies, which are recognisably (CH_3)–N values, a number of peaks appear which may well be various combinations of these modes between the two methyl groups present. The 1439, 1472 cm.$^{-1}$ features in the liquid, which are $d(CH_3)$ centres, form peaks on an absorption whose breadth indicates the

FIG. 11. *Infrared spectrum of* NN-*dimethylhydroxylamine vapour at* 98° *in the region* 4000—400 *cm.*$^{-1}$.



presence of more than two frequencies. It could be that the breadth arises from the coupling of the $d(CH_3)$ modes of the two methyl groups, but this seems unlikely in view of the normal width of the same two overlapping absorptions in the vapour. Accordingly, as the very strong d(OH) absorption in the vapour at 1312 cm.$^{-1}$ almost completely disappears in the liquid (a small peak appears at 1313 cm.$^{-1}$ which could be a combination tone, *e.g.*, 807 + 501 cm.$^{-1}$), it is natural to suggest that d(OH) in the liquid is under the $d(CH_3)$ absorptions and may have its centre in the shoulder seen at 1419 cm.$^{-1}$. However, an alternative is that the absorption at 1655 cm.$^{-1}$, which is very obvious in the liquid but has no counterpart in the vapour, is the d(OH) in the condensed phase. This would mean an exceptionally large displacement from the vapour (1655—1312 cm.$^{-1}$), but the intensity of the 1655 cm.$^{-1}$ feature in the liquid is difficult to account for unless it in some way involves the OH group. It could perhaps be a combination of d(OH) in the liquid with a low deformation mode (*ca.* 250 cm.$^{-1}$), *e.g.*, the torsional or other vibration of the associated OH group.

The vapour absorption at 1199 cm.$^{-1}$ (1204 cm.$^{-1}$, liq.) is somewhat stronger than one at 1154 cm.$^{-1}$ (1170 cm.$^{-1}$, liq.): although the former has a hybrid and somewhat irregular contour (partly, it seems, from overlap with the 1154 cm.$^{-1}$ band), the latter is of a distinctly *C*-character. These are two methyl modes, the wagging and the rocking vibration: in dimethylcyanamide, where the $(CH_3)_2N$ grouping also occurs, the absorptions are at 1205 and 1146 cm.$^{-1}$. Unless there is no coupling between the methyl groups, these two modes should each be double. No obvious signs of such coupling between the internal modes of the CH_3 groups are found in the spectrum, but this by no means precludes its occurrence for the external modes. At 1089 and 1069 cm.$^{-1}$ in the vapour (1090 and 1054 cm.$^{-1}$ in the liquid) there are weak absorptions which could well be the other members of the pairs of wagging and rocking modes. The further specification of these absorptions is speculative.

In the region of the skeletal stretching frequencies three absorptions are found at 999,

956, and 801 cm.$^{-1}$ in the liquid and at closely similar values in the vapour where their contours are *A* (or *AB*), *C*, and *C*. An appropriate pyramidal molecule for comparison with the dimethylhydroxylamine is trimethylamine.[13] In the latter the symmetric C–N stretching frequency is at 825 cm.$^{-1}$, the doubly degenerate antisymmetric stretching is at 1036 cm.$^{-1}$. Accordingly, 801 cm.$^{-1}$ in dimethylhydroxylamine corresponds to the former, and the 999 and 956 cm.$^{-1}$ features are antisymmetric stretching modes. An alternative description is to take the 999 and 801 cm.$^{-1}$ frequencies as ν_{as}(CNC) and ν_{sym}(CNC) [cf. 1070 and 780 cm.$^{-1}$ in $(CH_3)_2N{\cdot}CN$], with the 956 cm.$^{-1}$ absorption as essentially ν(NO) [cf. what has been described as ν(NO) in $NH_2{\cdot}O{\cdot}CH_3$ at 858 cm.$^{-1}$; in $CH_3{\cdot}NH{\cdot}OH$ at 950 cm.$^{-1}$; in $CH_3{\cdot}NH{\cdot}O{\cdot}CH_3$ at 933 cm.$^{-1}$].

The one strong absorption in the KBr region is at 501 cm.$^{-1}$ (liq). It is probably a bending of the skeleton [cf. similar vibrations in $(CH_3)_3N$ at 423 cm.$^{-1}$ (Raman) and in $(CH_3)_2N{\cdot}CN$ at 630 cm.$^{-1}$]. Other fundamentals are either too weak to be observed or occur outside the observed frequency range.

Trimethylhydroxylamine.—The volatility of this compound (b. p. 30°) meant that the liquid spectrum could not readily be recorded at room temperature and so the observations were for a 0·73M-solution in carbon tetrachloride (2000—900 cm.$^{-1}$) and for the vapour. Of the 36 normal modes, 27 will arise from methyl-group motions; the remaining nine will consist of four bond-stretching modes and five angular deformations of the (C_2NOC) skeleton. The uncertainty in the coupling of the various group frequencies makes the interpretation of band contours in terms of molecular conformation impossible.

In the 3 μ region, no less than seven distinct absorptions are found in the carbon tetrachloride solution of trimethylhydroxylamine. These can be designated as in Table 5 by reference to the other molecules in this series. In the vapour (Fig. 12), the rotational wings acquired by the vibrational stretching frequencies cause much overlapping of the component absorptions. There is much less suggestion of differentiation between the CH_3 groups in the deformation modes. Two clearly defined centres in the solution spectrum at 1470 and 1446 cm.$^{-1}$ correspond to the two peaks at 1477 and 1451 cm.$^{-1}$ which are the only features distinguishable in the vapour. There is also marked simplicity in the form of the rocking CH_3 frequencies near 1200 cm.$^{-1}$.

Four bands at 1060, 1005, 941, and 775 cm.$^{-1}$ have their counterparts at 1052, 991, and 934 cm.$^{-1}$ in carbon tetrachloride, which itself absorbs strongly below 850 cm.$^{-1}$. Consideration of the alternatives, and more particularly of the intensities, suggests that these

TABLE 5. *Infrared absorption frequencies (cm.$^{-1}$) in trimethylhydroxylamine.*

Soln. in CCl_4	Vapour	Assignment
	3000	
2987s	2989 s	$\nu_{as}(CH_3)$–N
	2966	
2957s	2953s	$\nu_{as}(CH_3)$–O
2939		
2894s	2893s	$2d_{as}(CH_3)$?
2864s	2874s	$2d_{sym}(CH_3)$?
2811m	2819ms	$\nu_{sym}(CH_3)$–O
2777(sh)	2787 m	$\nu_{sym}(CH_3)$–N
2769m	2776	
1470ms	1477ms	$d_{as}(CH_3)$
1447ms	1451ms	$d_{sym}(CH_3)$
1211m	1214m	wag.(CH_3)–O
1198(sh)		wag.(CH_3)–N
1154m	1155m	rock.(CH_3)–N
1086m		rock.(CH_3)–O?
	1070	
1052vs	1060 vs	skeletal stretching: out-of-phase $[\nu_{as}(CNC) + \nu_{as}(CON)]$?
	1054	
991m	1005w	skeletal stretching: in-phase $[\nu_{as}(CNC) + \nu_{as}(CON)]$?
934ms	941ms	skeletal stretching: $[\nu_{sym}(CNC)]$?
	782	
	775 ms	skeletal stretching: $[\nu_{sym}(CON)]$?
	766	
	532vw	skeletal deformation

stretching frequencies can be described as follows. The (C′NC″) group contributes a ν_{as}(C′NC″) and ν_{sym}(C′NC″) mode, and the adjacent (NOC″) group has two similar modes. The two-component three-particle antisymmetric modes give rise to frequencies which

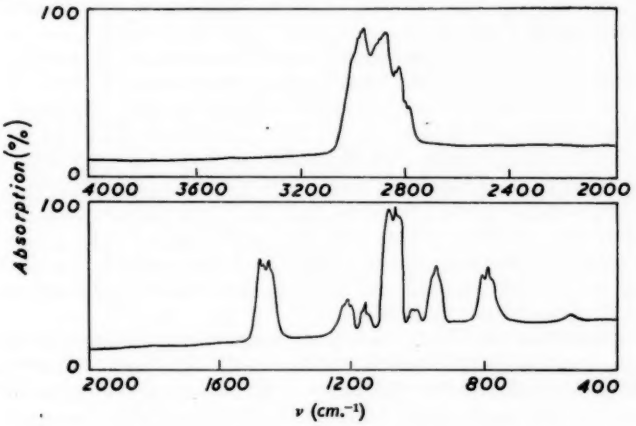
[13] Navech, Mattis, and Noël-Mathis, *Compt. rend.*, 1957, **244**, 1913; Edsall, *J. Chem. Phys.*, 1937, **5**, 225.

are close together, and one molecular mode will consist of their vibrations being in-phase, another of their out-of-phase motions. These can plausibly be assigned the 1059 and 1003 cm.$^{-1}$ frequencies. The remaining bands are due to the two three-particle " symmetric " vibrations; there is possibly only slight coupling between these frequencies, as 775 cm.$^{-1}$ is close to ν_{sym}(C'NC'') in dimethylcyanamide (767 cm.$^{-1}$) and in *NN*-dimethylhydroxylamine (776 cm.$^{-1}$).

The one absorption in the KBr region, at 522 cm.$^{-1}$, matches the similar feature in *NN*-dimethylhydroxylamine: it is quite possibly *d*(C'NC'') in both these cases.

General Conclusions.—The accumulated data suggest a picture of the hydroxylamines as a group of molecules conforming to normal single-bond conditions. Both the observed contours and the N–H frequencies (where they occur) confirm a pyramidal (sp^3) conformation of the nitrogen valencies, and the bond frequencies emphasize the essentially single-bond character of the molecules. This condition predisposes the structures to free rotation around the N–O bond, and a feature of particular interest is the preferred orientation assumed in these circumstances.

FIG. 12. *Infrared spectrum of trimethylhydroxylamine vapour at 25° in the region 4000—400 cm.$^{-1}$.*



Essentially skew structures are found in the parent hydroxylamine and the related hydrogen peroxide and hydrazine, and the evidence is fairly conclusive that two conformations are present in the vapour state of hydroxylamine itself. A similar condition is very likely for a number of the methylhydroxylamines. Suggestive evidence for two structures' being present in the vapour is shown by the doubling of particular absorption

TABLE 6. *Simplified stretching frequencies (vapour values) in the methylhydroxylamines (cm.$^{-1}$).*

Hydroxylamine	ν(C–O)	ν(C–N)	ν(N–O)
O-Methyl	998		858
N-Methyl		1032	950
ON-Diimethyl	1062	1022	933
NN-Dimethyl		900 *	950
Trimethyl	1005	917	941

* Mean of proposed ν_{as}(CNC) and ν_{sym}(CNC) values.

centres in the *O*-methyl and the *NN*-dimethyl compound and, with less weight, also in the *N*-methylhydroxylamine. In these cases there is strong probability that one (and maybe the principal) form is a " staggered *trans* " or skew conformation about the N–O bond.

There is also spectroscopic evidence for a *trans*-form of the skeleton in the *ON*-dimethyl compound, and normal van der Waals radii give the *trans*-orientation distinct preference for the trimethylhydroxylamine. Both general considerations and the existence of

TABLE 7. *Methyl-group frequencies in the substituted hydroxylamines.*

	O-Methyl	*N*-Methyl	*ON*-Dimethyl	*NN*-Dimethyl	Trimethyl
$\nu_{as}(CH_3)$–O	2938	—	2939	—	2939
$\nu_{sym}(CH_3)$–O	2811	—	2809	—	2811
$\nu_{as}(CH_3)$–N	—	2958	2977	2985 2946	2987 2957
$\nu_{sym}(CH_3)$–N	—	2784	2775	2774	2777 2769
$d_{as}(CH_3)$	1464	1469	1476 1460	1472	1470
$d_{sym}(CH_3)$	1438	1440	1441	1439	1447
Wagging (CH_3) out-of-plane	1212	1208	1219 1184	1204	1211 1198
Rocking (CH_3) in-plane	1143	1143	1153 1133	1170 1161	1154 1086(?)

alternative forms indicate that only small energy differences arise on rotation of these structures about the N–O bond.

Even the simplest of these compounds has a three-atom (NOC or CNO) framework, which means that coupling between its component vibrations will occur in the observed frequencies. It is significant that, despite this, no skeletal stretching mode has a frequency above 1070 cm.$^{-1}$, a limitation which shows the C–O, C–N, and N–O bonds concerned to be essentially single. To illustrate this aspect of the results one can make the drastic simplification of assuming that in (NOC) the higher stretching frequency is ν(C–O), and that in (CNO) it will be ν(C–N), then the frequencies are as in Table 6. Apart from establishing values close to those normal for such single bonds, the simplification of Table 6 shows the limitations of " characteristic bond frequencies." In all these instances the vibrations are not only of similar frequencies but are linked through common atoms so that isolated modes cannot be expected.

It is well known that the X–H modes are amongst the most constant of characteristic frequencies owing to the isolation of the motion of the hydrogen. This is borne out by the frequencies associated with the CH_3 group. The frequencies in Table 7 show a remarkable consistency. The small shifts in the stretching frequencies between (CH_3)–O and (CH_3)–N are, in fact, merely an expression of the slightly greater splitting between the antisymmetric and symmetric modes when the methyl group is attached to nitrogen. The arithmetic means of the two frequencies are: for the (CH_3)–O groups 2875, 2874, 2875 cm.$^{-1}$; for the (CH_3)–N groups, 2871, 2876, 2870, 2873 cm.$^{-1}$. Thus no difference in the C–H bonds is observed on this criterion.

It is perhaps even more surprising that the $d(CH_3)$ modes show such constancy, since, as judged from the methyl halides, these modes (and especially d_{sym}) are much more sensitive to changes in the attachment of the methyl radical. However, there are indications that it is the mass factor associated with X in CH_3–X which is significant in this respect.[14] Even so, it is remarkable that such little splitting of these modes occurs when two or more groups are present—so little that the vapour bands frequently appear as single well-defined modes. This simplicity is further emphasized by the similar behaviour of the CH_3 wagging and rocking modes.

Thus the general conclusion from this study of the methylhydroxylamines is that they show the simple structural relations expected from their " classical " single-bond formulæ. The adjacent C–N, C–O, and N–O bonds show no signs of those interactions so characteristic of amide structures, a condition which arises from the sp^3 hybridization of both carbon

[14] Davies and Hallam, *Trans. Faraday Soc.*, 1951, **47**, 1170.

and nitrogen atoms in those compounds but is precluded in the hydroxylamines by the essentially sp^3 valency states of the atoms.

Experimental

The spectra were obtained by using the Grubb-Parsons G.S.2 double-beam grating spectrometer from 4000 to 650 cm.$^{-1}$, and the S.3 single-beam with KBr prism from 700 to 420 cm.$^{-1}$. The calibration of the former was checked by using Plyler's values for polystyrene film, and the KBr range from well-established frequencies [15] in CO_2, CCl_4, PhMe, and $CHBr_3$. Conventional liquid cells and an 8 cm. gas cell which could be heated uniformly were available.

O-Methylhydroxylamine was prepared by the sequence: [16]

(i) $NaNO_2 + 2NaHSO_3 \longrightarrow HO{\cdot}N(SO_3Na)_2 + NaOH$
(ii) $HO{\cdot}N(SO_3Na)_2 + 2KCl \longrightarrow HO{\cdot}N(SO_3K)_2 + 2NaCl$
(iii) $HO{\cdot}N(SO_3K)_2 + Me_2SO_4 \longrightarrow MeO{\cdot}N(SO_3K)_2 + MeHSO_4$
(iv) $MeO{\cdot}N(SO_3K)_2 + 2H_2O \longrightarrow MeO{\cdot}NH_2 + 2KHSO_4$

The yield of disulphonate (ii) is poor and the methylation (iii) proceeds in cold alkaline solution. The free base (iv) is liberated by potassium hydroxide and distilled in steam, being carefully trapped in ice-cold hydrochloric acid. After evaporation and recrystallization from ether–ethanol the hydrochloride melted at 148°. The latter is treated with saturated aqueous sodium hydroxide in a small well-cooled flask which is gradually heated on a water-bath. The vapour passes through a column packed with sodium hydroxide pellets at 80°; repetition of this distillation gives a liquid of b. p. 48—49° (lit.,[2] 48·1°).

N-Methylhydroxylamine was obtained as its hydrochloride by Beckmann's method of reduction of methyl nitrate below 15°,[17] and recrystallized from ethanol–ethyl acetate until of m. p. 87°. Beckmann's procedure for separating the free base was found to be inefficient. The *dry* methanolic solution of the base (hydrochloride + NaOMe and filter) was placed in a small Claisen flask, an ice-cooled condenser attached, and the methanol slowly distilled through at *ca.* 25 mm. to a receiver in acetone–carbon dioxide. The solid residue subsequently was distilled to a new receiver on gently raising the temperature to 60° at 15 mm. Several such distillations failed to raise the m. p. above 38° (Beckmann gives 42°) but this agreed with that given by American workers [2] (38·5°).

The product was kept in a refrigerated desiccator and handled in a dry-box. Any specimen kept at room temperatures for 24 hr. or more was redistilled before use.

ON-Dimethylhydroxylamine was prepared *via* hydroxyurethane [16a] which was methylated: [18]

$NH_2{\cdot}OH + Cl{\cdot}CO_2Et \longrightarrow NH(OH){\cdot}CO_2Et + HCl$
$NH(OH){\cdot}CO_2Et + Me_2SO_4 \longrightarrow Me{\cdot}N(OMe){\cdot}CO_2Et$
$Me{\cdot}N(OMe){\cdot}CO_2Et \longrightarrow Me{\cdot}NH{\cdot}OMe + CO_2 + EtOH$

The fraction of *ON*-dimethylhydroxyurethane distilling at 150—155°/750 mm. was hydrolysed with potassium hydroxide in 50% ethanol and steam-distilled into ice-cold hydrochloric acid. Recrystallized from ethanol–ether, the hydrochloride had m. p. 115—116°. The free base (b. p. 42—43°) was obtained by the same procedure as for *O*-methylhydroxylamine but with potassium instead of sodium hydroxide.

NN-Dimethylhydroxylamine was prepared as its hydrochloride from ethyl nitrate: [19] m. p. after recrystallization, 103—106°. Bissot, Parry, and Campbell's prodecure using sodium-dried liquid ammonia was found the most efficient to separate the base: b. p. 100° (lit.,[2] 100·7°).

Trimethylhydroxylamine was obtained by methylation of the *ON*-dimethyl compound.[20] Phenyl isocyanate was used in separating the product, and dry hydrogen chloride was passed slowly, with cooling, into the ethereal distillate; recrystallized from ethanol–ether, the hydrochloride had m. p. 123°. This was placed on top of a few ml. of saturated aqueous potassium

[15] See Grubb-Parsons' Manual.
[16] (*a*) Jones, *Amer. Chem. J.*, 1898, **20**, 40; (*b*) Rashig, *Ber.*, 1907, **40**, 4580.
[17] Beckmann, *Annalen*, 1909, **365**, 204.
[18] Major and Fleck, *J. Amer. Chem. Soc.*, 1928, **50**, 1479.
[19] Hepworth, *J.*, 1921, **119**, 255.
[20] Jones and Major, *J. Amer. Chem. Soc.*, 1928, **50**, 2742.

XUM

hydroxide frozen by acetone–carbon dioxide in a small flask connected through an inverted U-shaped condenser-tube to a vapour trap containing anhydrous baryta. The latter was cooled to −20°, and the reaction flask warmed gently to about 30° after the system had been sealed under vacuum. After separation of the free base in this way, it was stored for 24 hr. over the drying agent and redistilled *in vacuo*: its normal b. p. was 29—30° (lit.,[2] 30°).

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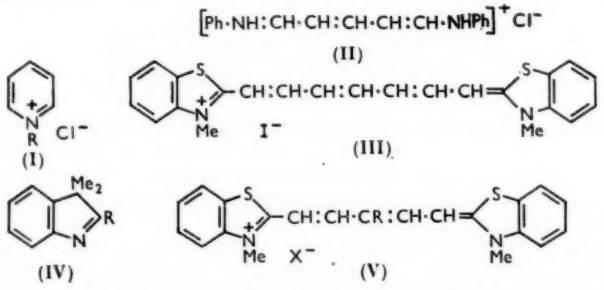
800. *A Novel Reaction of the Pyridine Ring.*

By G. E. FICKEN and J. D. KENDALL.

The preparation of 2-chloro-3,3-dimethylindolenine from 3,3-dimethyloxindole is described. The chloroindolenine, when treated in pyridine with a 2-methylbenzothiazole quaternary salt, gives, not the expected heptamethincyanine, but a pentamethincyanine. The mechanism of this reaction is discussed.

THE pyridinium ring in certain pyridine quaternary salts can be readily ruptured with the formation of glutaconaldehyde or derivatives thereof; *e.g.*, Zincke, Heuser, and Möller [1] showed that the quaternary salt (I; R = 2,4-dinitrophenyl) gave glutaconaldehyde dianil hydrochloride (II) when treated with aniline. A recent comprehensive review [2] of these reactions deals also with the closely related reaction whereby a heptamethincyanine (tricarbocyanine), *e.g.*, (III), can be formed directly from some pyridine quaternary salts by reaction under alkaline conditions with a heterocyclic quaternary salt possessing a reactive methyl group. The quaternary salt (I; R = 2,4-dinitrophenyl) was originally used for this purpose,[3] and one of the present authors [4] described a similar reaction with a salt (I; R = 2-benzoxazolyl). In these reactions glutaconaldehyde was assumed to be a transient intermediate.



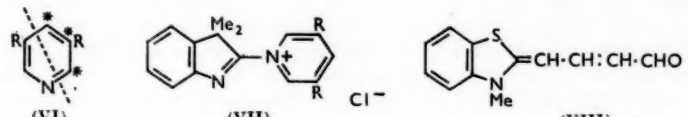
We have prepared 2-chloro-3,3-dimethylindolenine (IV; R = Cl) by reaction of 3,3-dimethyloxindole with phosphorus pentachloride. This chloroindolenine has a very reactive halogen atom and reacts rapidly with water and with aniline to yield 3,3-dimethyloxindole and 2-anilino-3,3-dimethylindolenine (IV; R = NHPh) respectively. There is

[1] Zincke, Heuser, and Möller, *Annalen*, 1904, **333**, 296.
[2] Creyf and Roosens, *Ind. chim. belge*, 1958, **23**, 855, 967; cf. Mosher, in Elderfield's "Heterocyclic Compounds," John Wiley and Sons, Inc., New York, 1950, Vol. I, p. 421.
[3] Wahl and I.G. Farbenindustrie A.-G., G.P. 499,967/1928; Fisher and Hamer, *J.*, 1933, 189.
[4] Kendall, B.P. 424,264/1933.

ready reaction when it is heated with 2,3-dimethylbenzothiazolium toluene-*p*-sulphonate in pyridine, but the product is the pentamethincyanine and not the expected heptamethincyanine (III). Isolated as its iodide, this product proved to be identical with the dye (V; R = H) prepared by treating 2,3-dimethylbenzothiazolium iodide with β-anilinoacraldehyde anil hydrochloride.[5]

This unexpected reaction involves the pyridine ring, since with 3,5-lutidine in place of pyridine the chain-substituted pentamethincyanine (V; R = Me) was obtained. This result indicated that the pyridine ring had split as shown in (VI), the carbon atoms marked * providing the three central atoms of the pentamethin chain. The fate of the remaining two carbon atoms is unknown. The reaction, involving cleavage of a carbon–carbon link under very mild conditions is apparently without parallel in the pyridine series, and the mechanism is by no means clear. Certainly it involves preliminary formation of pyridinium quaternary salts of type (VII), since these can be isolated; although these quaternary chlorides could not be obtained pure, a pure crystalline perchlorate was obtained on reaction of the salt (VII; R = H) with aqueous sodium perchlorate. Reaction with the benzothiazole quaternary salt in pyridine then leads to dyes (V; R = H and Me) from the quaternary salts (VII; R = H and Me respectively). However, with aniline in pyridine, the salt (VII; R = H) gives Zincke's salt (II) so that the pyridine ring has here split in the normal manner. Moreover, if the reaction of quaternary salt (VII; R = H) with the benzothiazole quaternary salt is carried out in ethanolic sodium ethoxide the chief product is the heptamethincyanine (III), the pentamethincyanine being a minor product; here also normal ring opening has occurred.

Clearly, the indoleninylpyridinium chloride (VII; R = H) can react with 2,3-dimethylbenzothiazolium toluene-*p*-sulphonate in two different ways: first, by a normal reaction leading to heptamethincyanine, and presumably involving an initial fission of the pyridine ring with the formation of glutaconaldehyde, under the action of a strong base (sodium ethoxide). In the more feebly basic pyridine, this ring opening to glutaconaldehyde does not occur, and the " abnormal " reaction supervenes; this presumably involves reaction of the benzothiazole quaternary salt (or the related methylene base) with the pyridinium



(VI) (VII) (VIII)

salt before ring opening occurs. Normally, reaction at the 2-position of the pyridine ring might be expected to occur, leading eventually to a heptamethincyanine. In the case of the indoleninylpyridinium salts (VII), however, this evidently does not happen, owing possibly to steric hindrance by the *gem*-dimethyl group of the indolenine ring. Reaction of the benzothiazole salt at the 4-position of the pyridine residue in salt (VII) must be assumed to occur in this case, followed by fission of the pyridine ring as in (VI) to give an intermediate, possibly (VIII), which could react with a further molecule of benzothiazolium salt to give a pentamethincyanine.

The reaction of the chloroindolenine with 2,3-dimethylbenzothiazolium toluene-*p*-sulphonate in a number of other pyridine bases has been examined. Only with β-picoline was evidence for the formation of a dicarbocyanine obtained. With α- and γ-picoline, 2,6-lutidine, and 2,4,6-collidine no dicarbocyanine could be detected in the mixture of dyes formed, owing, presumably, to the presence of reactive methyl groups in these compounds. We have also attempted to extend the scope of the reaction by the use of other reactive halogen compounds in place of the chloroindolenine. Spectroscopic evidence

[5] Piggott, Rodd, and I.C.I. Ltd., B.P. 355,693/1930.

for the formation of a pentamethincyanine was obtained in the reaction of 1-chloro-2,4-dinitrobenzene and of 2-chlorobenzothiazole with 2,3-dimethylbenzothiazolium toluene-*p*-sulphonate in pyridine: however, in both cases a mixture of dyes was formed and no pure material could be isolated.

Experimental

2-Chloro-3,3-dimethylindolenine.—A mixture of 3,3-dimethyloxindole [6] (50 g.) and phosphorus pentachloride (100 g., 1·5 mol.) was heated under reflux at 150—160° for 1 hr., by which time evolution of hydrogen chloride had practically ceased. As much volatile material as possible (mostly phosphoryl chloride) was then distilled off, the temperature of the bath being raised finally to 180°. The residue was then fractionated, to give fractions (i), b. p. 121—124°/22 mm. (36·7 g., 66%), and (ii) b. p. 140°/22 mm. to 160°/26 mm. (12·3 g.). Fraction (i) consisted of *2-chloro-3,3-dimethylindolenine*, which was obtained as a fuming liquid, b. p. 114°/16 mm., n_D^{16} 1·5542 (Found: C, 66·3; H, 5·4. $C_{10}H_{10}NCl$ requires C, 66·8; H, 5·6%). The second fraction was a mixture, but was probably largely a *2,x*-dichloro-3,3-dimethylindolenine. Use of equimolecular quantities of oxindole and phosphorus pentachloride led to incomplete reaction of the oxindole, whilst increase of the proportion of phosphorus pentachloride to 2 mols. increased the amount of high-boiling material at the expense of the chloroindolenine. The infrared spectrum of the chloroindolenine showed the following bands: 3070 and 2970 (CH stretch), 1720 (C=N stretch), 1590 (C=C stretch), 1550s, 1465 and 1450s (C=C stretch), 1380 and 1360 (CH deformation of *gem*-dimethyl group), 1330, 1305, 1260, 1210s, 1190, 1155, 1120, 1090, 1035s, 1015s, 990, 947, 869, 852, 827, 770s, 756s (CH out-of-plane deformation of *ortho*-disubstituted benzene), 687 cm.$^{-1}$.

Reactions of the Chloroindolenine.—When the chloroindolenine was warmed briefly with aqueous sodium carbonate a white solid was formed. After crystallisation from ethyl acetate, this had m. p. 149—150° alone or mixed with 3,3-dimethyloxindole (m. p. 151°).

The chloroindolenine (2·2 g.) was added to a solution of aniline (2·5 g.) in dry ether (20 ml.). After 2 hr. at room temperature, the ether was boiled off and the residue was washed with dilute hydrochloric acid and triturated with dilute aqueous sodium hydroxide solution. The product (2·71 g.) had m. p. 160—166°, and by successive crystallisations from aqueous ethanol and from cyclohexane, followed by sublimation under reduced pressure, yielded *2-anilino-3,3-dimethylindolenine*, m. p. 169—170° (Found: C, 81·0; H, 6·7. $C_{16}H_{16}N_2$ requires C, 81·3; H, 6·8%).

A mixture of the chloroindolenine (3·5 g.) and dry pyridine (1·7 g.) was kept at room temperature for 16 hr. Addition of ether gave a solid which was washed successively with ether, acetone, and ethyl acetate to leave the quaternary chloride (VII; R = H) as a dark, deliquescent solid. A solution in a little hot water was treated with charcoal and filtered into an aqueous solution of sodium perchlorate. The precipitate was washed with a little cold water and crystallised from water, to yield *1-(3,3-dimethyl-2-indoleninyl)pyridinium perchlorate* as pale yellow needles, m. p. 199—201° (Found: Cl, 11·15. $C_{15}H_{15}O_4N_2Cl$ requires Cl, 11·0%). Reaction of the chloroindolenine with 3,5-lutidine similarly gave the quaternary salt (VII; R = Me).

Reaction of the Chloroindolenine with Pyridine, etc., and 2,3-Dimethylbenzothiazolium Toluene-p-sulphonate.—(a) *Pyridine.* The chloroindolenine (0·90 g.) was added to a suspension of finely powdered 2,3-dimethylbenzothiazolium toluene-*p*-sulphonate (1·40 g.) in dry pyridine (10 ml.). After 10 days in a stoppered flask at room temperature, the mixture was added to a warm concentrated solution of potassium iodide in water. The precipitated dye was washed with boiling water, then with hot ethanol until the washings were pure blue (much brown material was removed). The residue was almost pure bis-(3-methyl-2-benzothiazole)pentamethincyanine iodide (0·70 g.), m. p. 286—288° (decomp.), and the cooled ethanol washings deposited a further crop (0·11 g.) of slightly less pure material (total yield 79%). The dye formed blue-green needles, m. p. 292—293° (decomp.) (Kendall [7] gives m. p. 281°), from 2-methoxyethanol (730 ml./g.) (Found: N, 6·0; S, 13·0; I, 25·6. Calc. for $C_{21}H_{19}N_2S_2I$: N, 5·7; S, 13·2; I, 25·9%), $\lambda_{max.}$ (in 2-methoxyethanol) 6525 Å (log ε 5·30) (Hamer and Rathbone [8] give $\lambda_{max.}$ 6500 in methanol). The dye was identical with that prepared in 40% yield by refluxing 2,3-dimethylbenzothiazolium iodide (1·46 g.) with β-anilinoacraldehyde anil hydrochloride (0·65 g.) in

[6] Brunner, *Monatsh.*, 1906, **27**, 1183.
[7] Kendall, B.P. 431,186/1933.
[8] Hamer and Rathbone, *J.*, 1945, 595.

ethanol (50 ml.) containing triethylamine (2·5 ml.) for 1 hr. The dyes had identical m. p.s and mixed m. p., although mixed m. p.s are unreliable in this series. However, the dyes proved to be identical also in their appearance, solubility, and light absorption, both in the visible and in the infrared region (2·5—15 μ). These criteria were also used in every other case to prove the identity of a pair of dyes.

(b) **3,5-*Lutidine*.** The sample of base used was estimated by vapour-phase chromatography to have a 3,5-lutidine content of at least 99·5%. The dried (KOH) material distilled completely at 170—171°/765 mm. (Coulson and Ditcham [9] give b. p. 169—170°/767 mm.); the picrate had m. p. 238° and the methiodide, m. p. 274° (Oparina [10] gives m. p.s 238 and 275°, respectively). A mixture of 2,3-dimethylbenzothiazolium toluene-*p*-sulphonate (1·70 g.), 3,5-lutidine (2·0 ml.), and 2-chloro-3,3-dimethylindolenine (0·55 g.) was warmed on the steam-bath for 1½ hr., by which time much dye had crystallised. The mixture was boiled with methanol (20 ml.), and the dye (0·60 g., 44%) was filtered off after cooling. This proved to be *bis*-(3-*methyl*-2-*benzothiazole*)-γ-*methylpentamethincyanine toluene*-p-*sulphonate*, m. p. 239° (from methanol, 100 ml.), green needles (Found: C, 62·8; H, 5·6; N, 5·0; S, 16·7. $2C_{29}H_{28}O_3N_2S_3,CH_4O$ requires C, 62·7; H, 5·35; N, 5·0; S, 17·0%). A solution of the dye in warm 2-methoxyethanol was treated with aqueous potassium iodide solution to yield the *iodide*, blue-green needles, m. p. 283—284° (decomp.) (from 2-methoxyethanol, 175 ml./g.) (Found: C, 52·6; H, 4·7; N, 5·7; S, 12·8; I, 24·8. $C_{22}H_{21}N_2S_2I$ requires C, 52·4; H, 4·2; N, 5·6; S, 12·7; I, 25·2%), $\lambda_{max.}$ (in EtOH) 6510 Å (log ε 5·34). The dye was completely identical with that prepared as follows, by a modification of the method suggested by Ogata.[11] A mixture of 2-2′-ethylthiovinyl-3-methylbenzothiazolium iodide [12] (1·82 g.), methylmalonic acid (0·6 g.), and pyridine (30 ml.) was warmed on the steam-bath. After 1 hr. more methylmalonic acid (0·6 g.) was added and the mixture was refluxed for 1 hr. The crystals which separated on cooling were washed with ethanol to yield the dye (0·34 g.) which was obtained as blue-green needles (0·23 g.) from 2-methoxyethanol.

Reaction of Quaternary Pyridinium Salts with **2,3-*Dimethylbenzothiazolium Toluene*-p-*sulphonate*.**—(a) *In pyridine.* A mixture of 1-(3,3-dimethyl-2-indoleninyl)-3,5-dimethylpyridinium chloride (VII; R = Me) (1·0 g.) and 2,3-dimethylbenzothiazolium toluene-*p*-sulphonate (2·3 g.) in pyridine (5·0 ml.) was warmed on the steam-bath for 1 hr. The resulting solution was diluted to 25 ml. with ethanol, then filtered, and the filtrate was treated with aqueous potassium iodide. The precipitated dye crystallised from 2-methoxyethanol to yield bis-(3-methyl-2-benzothiazole)-γ-methylpentamethincyanine iodide, m. p. 283—284° (decomp.), identical with that prepared as described above. On use of 1-(3,3-dimethyl-2-indoleninyl)-pyridinium chloride (VII; R = H), the product was bis-(3-methyl-2-benzothiazole)pentamethincyanine iodide.

(b) *In sodium ethoxide solution.* A cold solution of 1-(3,3-dimethyl-2-indoleninyl)pyridinium chloride (VII; R = H) (0·47 g.) and 2,3-dimethylbenzothiazolium toluene-*p*-sulphonate (1·22 g.) in ethanol (15 ml.) was treated with cold sodium ethoxide solution (2 g. of sodium per 100 ml.; 4 ml.). After 30 min. a concentrated solution of potassium iodide (10 g.) in water was added, and the precipitated solid was washed with boiling water and crystallised from methanol (650 ml./g.) to yield dark green *bis*-(3-*methyl*-2-*benzothiazole*)*heptamethincyanine iodide* (0·23 g.), m. p. 216—217° (decomp.) (Found: C, 53·5; H, 4·5; S, 12·4. $C_{23}H_{21}N_2S_2I$ requires C, 53·5; H, 4·1; S, 12·5%), $\lambda_{max.}$ (in MeOH) 7520 Å (log ε 5·38). Evaporation of the mother-liquors from the recrystallisation to small volume yielded a solid (0·01 g.) which appeared spectroscopically to be largely pentamethincyanine. The heptamethincyanine was identical with the dye prepared by reaction of 1-2′-benzoxazolylpyridinium chloride with 2,3-dimethylbenzothiazolium toluene-*p*-sulphonate by Kendall's method.[4]

Reaction of Quaternary Salt (VII; R = H) *with Aniline.*—A mixture of the chloroindolenine (1·1 g.) and pyridine (5·0 ml.) was kept at room temperature for 3 hr. Addition of aniline (2·0 ml.) caused the solution to become deep red, and red crystals soon separated. After 30 min. these were filtered off and washed with a little ethanol, giving glutaconaldehyde dianil hydrochloride (1·09 g.) as red needles with a blue reflex, m. p. 153—154° undepressed on admixture with an authentic specimen.[1]

[9] Coulson and Ditcham, *J.*, 1957, 356.
[10] Oparina, *J. Russ. Phys. Chem. Soc.*, 1929, **61**, 2001; *Chem. Abs.*, 1930, **24**, 3790.
[11] Ogata, *Bull. Inst. Phys. Chem. Res. Japan*, 1937, **16**, 631.
[12] Kendall and Majer, *J.*, 1948, 687.

The visible spectra were measured on a Unicam SP. 500 spectrophotometer, and the infrared spectra on an Infracord spectrophotometer, model 137.

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ILFORD, ESSEX. [*Received, May 27th*, 1959.]

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801. *Syntheses of 1-Phenylfluorene and 1- and 3-Phenylphenanthrene.*

By D. M. W. ANDERSON, NEIL CAMPBELL, D. LEAVER, and (the late) W. H. STAFFORD.

The syntheses of these hydrocarbons and of *m*-terphenyl are reported. The spectra of these and related compounds are discussed.

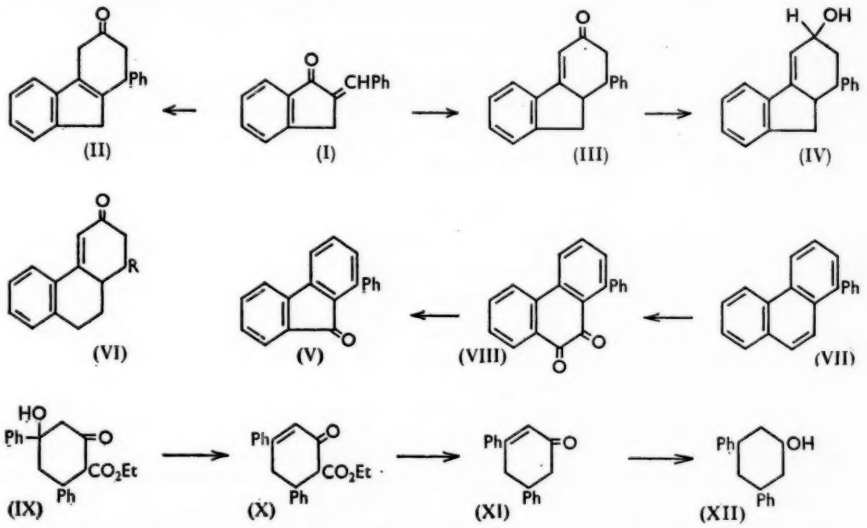
2-BENZYLIDENEINDAN-1-ONE (I) and ethyl acetoacetate with one mole of sodium ethoxide failed to yield the expected ethyl 1,2,3,9a-tetrahydro-3-oxo-1-phenylfluorene-2-carboxylate (a derivative of III), but gave instead an ester in which the 4,4a double bond had moved to the 4a,9a-position. An infrared band at 1670 cm.$^{-1}$ was shown not to be due to a conjugated carbonyl group [1] by the absence of an absorption band at 280—300 mμ such as is found in the spectrum of 3,5-diphenylcyclohex-2-en-1-one (XI). The structure of this and related esters will be discussed later.

The ester when heated with sulphuric acid, acetic acid, and water afforded 1,2,3,4-tetrahydro-3-oxo-1-phenylfluorene (II), whose constitution follows from the similarity of its ultraviolet spectrum to those of β-methylstyrene and indene,[2a, b] and from a single infrared band at 1716 cm.$^{-1}$ denoting an unconjugated carbonyl group.[3] Slightly different conditions but no distillation yielded the isomeric 1,2,3,9a-tetrahydro-3-oxo-1-phenylfluorene (III), whose constitution follows from the similarity of its ultraviolet spectrum to that of benzylideneacetone [4a] and from infrared bands at 1650 cm.$^{-1}$ (with shoulder at 1670 cm.$^{-1}$ which is resolved into a peak at 1672 cm.$^{-1}$ by the use of hexachlorobutadiene) and 1622 cm.$^{-1}$. These are attributed to the conjugated carbonyl and ethylenic groups in the fragment CH:CH·CO· and are comparable with the carbonyl absorption band at 1650 cm.$^{-1}$ in benzylideneacetophenone and the ethylenic band at 1620 cm.$^{-1}$ in benzylideneindanone.[5] Similar instances of isomerism of unsaturated cyclic ketones have been reported,[4a, b] but whereas in some of these at least, double-bond migration is effected by alkali we found that mere distillation was sufficient to convert the αβ-isomer (III) partially into the βγ-isomer (II). Reduction of the ketone (III) with lithium aluminium hydride gave 1,2,3,9a-tetrahydro-3-hydroxy-1-phenylfluorene (IV),[6] which yielded 1-phenylfluorene (V; CH_2 instead of CO) by dehydration and dehydrogenation with sulphur. The structure of this compound was confirmed by oxidising it to 1-phenylfluorenone (V) [absorption at 1706 cm.$^{-1}$ comparable to 1718 cm.$^{-1}$ in fluorenone [7]].

By a similar series of reactions 2-benzylidenetetral-1-one yielded 1,2,3,9,10,10a-hexahydro-3-oxo-1-phenylphenanthrene (VI; R = Ph), absorbing at 1660 cm.$^{-1}$, reduced by

[1] Bellamy, "The Infrared Spectra of Complex Molecules," Methuen, London, 1956, p. 118.
[2] (*a*) Campbell, Linden, Godshalk, and Young, *J. Amer. Chem. Soc.*, 1947, **69**, 880; (*b*) Ramart-Lucas and Amagat, *Bull. Soc. chim. France*, 1932, **51**, 119.
[3] Ref. 1, p. 116.
[4] (*a*) Robinson *et al.*, *J.*, 1936, 752, 759; (*b*) Köster, *Ber.*, 1944, **77**, 553.
[5] Hassner and Cromwell, *J. Amer. Chem. Soc.*, 1958, **80**, 896.
[6] Cf. Keene and Schofield, *J.*, 1958, 1080.
[7] Bergmann and Pinchas, *J. Chim. Phys.*, 1952, **49**, 537; Josien and Fuson, *Bull. Soc. chim. France*, 1952M, 389.

lithium aluminium hydride to the alcohol (VI; R = Ph, with CH·OH for CO), whose ultraviolet spectrum resembled that of cinnamyl alcohol.[2a] The ketone was converted by sulphur into 1-phenylphenanthrene (VII).[8]



The Mannich base 2-morpholinomethyltetral-1-one was methylated and condensed with ethyl acetoacetate. The resulting keto-ester when distilled under reduced pressure gave 1,2,3,9,10,10a-hexahydro-3-oxophenanthrene (VI; R = H), with a broad band at 1660 cm.$^{-1}$, which with phenylmagnesium bromide gave the corresponding alcohol. Dehydration and dehydrogenation of the alcohol with sulphur yielded 3-phenylphenanthrene. All the monophenylphenanthrenes have now been synthesised.

Chalkone and ethyl acetoacetate interact in the presence of bases to give, according to the experimental conditions,[9] a 1,5-diketone, the isomeric ethyl 4-hydroxy-2-oxo-4,6-diphenylcyclohexanoate (IX), absorbing at 1706 cm.$^{-1}$ (6-membered ring ketone), 1748 cm.$^{-1}$ (non-enolised β-keto-ester), and 3390 cm.$^{-1}$ (OH with bonding), and ethyl 2-oxo-4,6-diphenylcyclohex-3-enoate (X), absorbing at 1735 cm.$^{-1}$ (ethoxycarbonyl group), 1663 cm.$^{-1}$ (αβ-unsaturated ketone), and 287 mμ (Ph·CH:CH·CO·CH_2· grouping). Hydrolysis and decarboxylation of the ester (X) gave 3,5-diphenylcyclohex-2-en-1-one (XI),[10] shown to be an αβ-unsaturated ketone by absorption at 285 mμ (log ε 4·27) and by an infrared band at 1657 cm.$^{-1}$. The compound (XI) when reduced to the alcohol (XII) and heated with sulphur yielded *m*-terphenyl.[11]

The absorption spectra of the phenylated hydrocarbons were compared with those of the parent hydrocarbons. The spectrum of 1-phenylfluorene resembles that of *m*-terphenyl but differs markedly from that of fluorene and 9-phenylfluorene (Fig. 1).[12] The spectra of fluorenone and 1-phenylfluorenone, however, display considerable similarity (Fig. 2). In the absence of data for other phenylated fluorenes and fluorenones discussion is not attempted.

Models show that the coplanarity of the rings in 1- and 9-phenylphenanthrene is opposed by steric interference and it might be expected that the spectra of these compounds [8,12]

[8] Fuson and Tomboulian, *J. Amer. Chem. Soc.*, 1957, **79**, 956.
[9] Dieckmann and v. Fischer, *Ber.*, 1911, **44**, 966.
[10] Petrov, *Ber.*, 1929, **62**, 642.
[11] Gillam and Hey, *J.*, 1939, 1170.
[12] Bradsher and Wissow, *J. Amer. Chem. Soc.*, 1946, **68**, 2149.

would be similar to one another and to that of phenanthrene [13] but differient from those of 2- and 3-phenylphenanthrene.[14] There is indeed such similarity if allowance is made for the lack of fine structure in the phenyl-phenanthrenes (see Table), but this cannot be

FIG. 1.

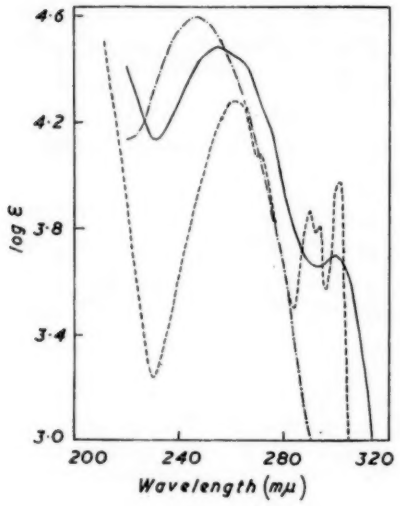


FIG. 2.

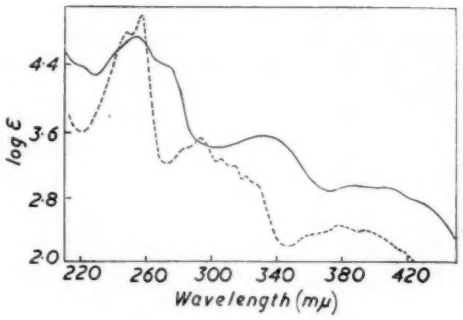


FIG. 1. *Ultraviolet absorption spectra, in ethanol, of fluorene* (– – – –), *1-phenylfluorene* (——), *and* m-*terphenyl* (— · — · —).

FIG. 2. *Ultraviolet absorption spectra, in ethanol, of fluorenone* (– – – –) *and 1-phenylfluorenone* (——).

FIG. 3.

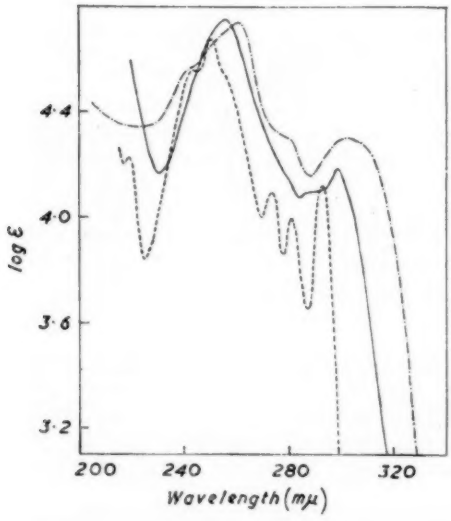


FIG. 4.

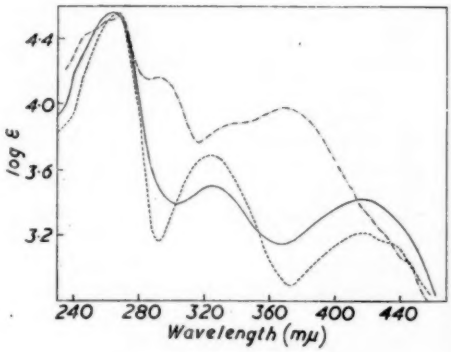


FIG. 3. *Ultraviolet absorption spectra, in ethanol, of phenanthrene* (– – – –), *1-phenylphenanthrene* (——), *and 3-phenylphenanthrene* (— · — · —).

FIG. 4. *Ultraviolet absorption spectra, in chloroform, of phenanthraquinone* (– – – –), *1-phenylphenanthraquinone* (——), *and 3-phenylphenanthraquinone* (— · — · —).

used as evidence for lack of conjugation since the spectra of 1- and 3-phenylphenanthrene (Fig. 3) are not very different. Evidently we are dealing with an instance of spectral conjugation without coplanarity.[15] The spectrum of 1-phenylphenanthraquinone [8] differs, however, from that of 3-phenylphenanthraquinone (Fig. 4).

[13] Jones, *J. Amer. Chem. Soc.*, 1945, **67**, 2021.

Spectra of Phenylphenanthrenes.

Position of Ph group	Unsub.[12] *	1 [8]	2 [14]	3	4 [13]	9 [11]
$\lambda_{max.}$ (mμ)	252	256	276	261	230	254
	293	298	291	302	258	298
	330					

* Highest peak.

4-Phenylphenanthrene [16] has a band at 230 mμ not observed in phenanthrene or the other phenylphenanthrenes, possibly a reflection of molecular overcrowding, and there are marked differences between the spectra of 2- and 3-phenylphenanthrenes although in these compounds the phenyl groups are free from steric interference.

Experimental

Ultraviolet spectra were measured with a Unicam SP. 500 quartz spectrophotometer and infrared spectra were obtained in Nujol mulls with a Hilger H 800 double-beam spectrometer. Ether extracts were dried (Na_2SO_4) and evaporated under reduced pressure. The light petroleum had b. p. 60—80°.

1,2,3,4-*Tetrahydro*-3-*oxo*-1-*phenylfluorene*.—2-Benzylideneindan-1-one (50 g.), ethyl acetoacetate (30 g.), and ethanol (250 ml.) containing sodium ethoxide (from 5 g. of sodium) were boiled for 3 hr. and poured into water (1 l.) containing acetic acid (15 ml.). Extraction with ether and evaporation gave a syrup (*A*) and an *ester* (46 g.), m. p. 133—134° after crystallisation from light petroleum (Found: C, 79·5; H, 6·0. $C_{22}H_{20}O_3$ requires C, 79·5; H, 6·1%); $\lambda_{max.}$ 218 and 253 mμ (log ε 4·40 and 4·34), ν 1670, 1637, and 1600 cm.$^{-1}$. The ester (2 g.) was boiled for 3 hr. with acetic acid (10 g.), sulphuric acid (8 g.), and water (8 g.) and the mixture then poured into water. The resulting yellow oil when triturated with ether yielded a polymer of 2-benzylideneindan-1-one probably the *dimer*, m. p. 244—245° (Found: C, 87·3; H, 5·8. $C_{32}H_{24}O_2$ requires C, 87·3; H, 5·5%). Evaporation of the ether extract gave a residue which when distilled at 230°/0·1 mm. yielded 1,2,3,4-*tetrahydro*-3-*oxo*-1-*phenylfluorene* as plates, m. p. 115°, from light petroleum; $\lambda_{max.}$ 261 mμ (log ε 4·12) in ethanol (Found: C, 87·5; H, 6·3. $C_{19}H_{16}O$ requires C, 87·7; H, 6·2%). The 2,4-*dinitrophenylhydrazone* formed red prisms, m. p. 236—237°.

1,2,3,9*a*-*Tetrahydro*-3-*oxo*-1-*phenylfluorene*.—The above ester (45 g.) was boiled (40 min.) with acetic acid (180 ml.), sulphuric acid (90 ml.), and water (45 ml.), and the mixture poured into water. Extraction with ether and evaporation of the ether gave 1,2,3,9*a*-*tetrahydro*-3-*oxo*-1-*phenylfluorene* (25 g.) as elongated plates (from light petroleum), m. p. 117—118° (depressing the m. p. of the isomer); $\lambda_{max.}$ 235, 291, and 313 mμ (log ε 3·98, 4·24, and 4·24) in ethanol (Found: C, 87·7; H, 6·2%). Some of the compound was obtained by similar hydrolysis and decarboxylation of the syrup (*A*). The 2,4-*dinitrophenylhydrazone* had m. p. 236—237°, not depressed when admixed with the dinitrophenylhydrazone obtained from the isomer (Found: C, 68·4; H, 4·5. $C_{25}H_{20}O_4N_4$ requires C, 68·2; H 4·4%). Distillation of the oxo-compound at 250°/0·01 mm. and recrystallisation of the distillate from ethanol–light petroleum gave mainly unchanged compound, but evaporation of the mother liquors yielded rectangular and hexagonal plates. The latter were separated by extraction with a little ether and afforded the isomeric βγ-unsaturated ketone, m. p. and mixed m. p. 115°.

1-*Phenylfluorene*.—Lithium aluminium hydride (1·4 g.) in ether was added to the ketone (III) (13·4 g.) in ether (250 ml.) and benzene (50 ml.), and the mixture was boiled (5 min.). Ammonium chloride solution was added; the ethereal layer on evaporation gave 1,2,3,9*a*-*tetrahydro*-3-*hydroxy*-1-*phenylfluorene* (11·5 g.) as needles, m. p. 100—101°, after trituration with light petroleum and crystallisation from benzene (Found: C, 87·2; H, 6·8. $C_{19}H_{18}O$ requires C, 87·0; H, 6·9%). This had a broad hydroxyl band at 3400—3100 cm.$^{-1}$ due to considerable hydrogen bonding. The alcohol (5·2 g.) was heated at 220° with sulphur (0·75 g.) for 3 hr., and the residue was chromatographed in light petroleum–benzene on alumina (200 g.). Development with light petroleum–benzene yielded 1-*phenylfluorene* (3·3 g.) as needles (from ethanol–light petroleum), m. p. 48° (Found: C, 94·2; H, 5·6. $C_{19}H_{14}$ requires C, 94·2; H, 5·8%); $\lambda_{max.}$

[14] Miller and Mann, *J.*, 1951, **73**, 45.
[15] Turner *et al.*, *J.*, 1952, 854.
[16] Campbell, *J.*, 1954, 3659.

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255 and 300 mμ (log ε 4·49 and 3·70) in ethanol. 1-Phenylfluorene (0·5 g.) was oxidised by chromium trioxide and acetic acid to 1-*phenylfluorenone* (0·1 g.), yellow needles (from ethanol), m. p. 120° (Found: C, 88·7; H, 4·7. $C_{19}H_{12}O$ requires C, 89·0; H, 4·7%); $\lambda_{max.}$ 253, 330, 385—390 mμ (log ε 4·74, 3·56, and 2·95) in 95% ethanol.

1,2,3,9,10,10a-*Hexahydro*-3-*oxo*-1-*phenylphenanthrene*.—A solution of 2-benzylidenetetral-1-one (100 g.) and ethyl acetoacetate (58·9 g.) in ethanol (600 ml.) containing sodium ethoxide (from 10 g. of sodium) was boiled for 4 hr. and worked up as above to give a syrup (B) and an *ester* (85 g.), pale yellow prisms, m. p. 141°, from light petroleum–ethyl acetate (Found: C, 79·5; H, 6·5. $C_{23}H_{22}O_3$ requires C, 79·7; H, 6·4%); $\lambda_{max.}$ 220 and 254 mμ (log ε 4·46 and 4·32); ν 1675, 1647, and 1627 cm.$^{-1}$. The ester (85 g.), acetic acid (320 g.), sulphuric acid (160 ml.), and water (80 ml.) were boiled (15 min.) and treatment as above yielded 1,2,3,9,10,10a-*hexahydro*-3-*oxo*-1-*phenylphenanthrene* (47 g.), also obtained (13 g.) by the hydrolysis and decarboxylation of syrup B; it formed pale yellow rhombs (from light petroleum–benzene), m. p. 99° (Found: C, 87·7; H, 6·8. $C_{20}H_{18}O$ requires C, 87·6; H, 6·6%); $\lambda_{max.}$ 229 and 300 mμ (log ε 4·03 and 4·32) in ethanol. The 2,4-*dinitrophenylhydrazone* formed red prisms, m. p. 272—274° (Found: C, 68·9; H, 4·9; N, 12·4. $C_{26}H_{22}O_4N_4$ requires C, 68·7; H, 4·9; N, 12·3%). A solution of the ketone (30 g.) in ether (400 ml.) and benzene (100 ml.) was boiled (10 min.) with lithium aluminium hydride (1·5 g.) in ether (100 ml.) yielding the *hexahydro*-3-*hydroxyphenanthrene* (30 g.), needles (from benzene), m. p. 120°, which loses benzene when heated (Found: C, 87·8; H, 7·4. $C_{20}H_{20}O,C_6H_6$ requires C, 88·1; H, 7·4%); $\lambda_{max.}$ 257, 288 (infl.), and 298 mμ (infl.) (log ε 4·12, 3·35, and 3·20).

1-*Phenylphenanthrene*.—The alcohol (5·5 g.) was heated at 220° (3 hr.) with sulphur (1·4 g.); the residue when chromatographed in light petroleum–benzene on alumina (200 g.) afforded 1-phenylphenanthrene (3·5 g.), plates, m. p. 79° (lit.,[17] m. p. 79—79·5°); $\lambda_{max.}$ 256 and 298 mμ (log ε 4·75 and 4·19). The picrate had m. p. 117° (lit.,[17] m. p. 117—117·5°), the quinone, m. p. 230—231° (lit.,[8] m. p. 230—231°); $\lambda_{max.}$ 264, 325, and 415 mμ (log ε 4·56, 3·50, and 3·42) in chloroform, whose azine absorbed at 255, 280 (infl.), 298, 311, 365, and 382 mμ (log ε 4·85, 4·63, 4·06, 4·06, 4·07, and 4·11). The quinone (0·5 g.) was heated with 10% aqueous ethanolic potassium hydroxide in a stream of air until it dissolved. The solution was acidified, extracted with ether, and the ethereal layer shaken with sodium carbonate solution. The aqueous layer with hydrochloric acid yielded 9-hydroxy-1-phenylfluorene-9-carboxylic acid, which was heated at 220—230° until evolution of gas ceased. The resulting brown oil was heated (1 min.) with chromium trioxide ("AnalaR"; 0·4 g.) in acetic acid and the solvent then evaporated under reduced pressure. The residue was shaken with ether and water; evaporation of the ethereal layer gave a yellow oil which after chromatographic purification gave 1-phenylfluorenone, m. p. and mixed m. p. with the above sample, 120°.

3-*Phenylphenanthrene*.—A solution of α-tetralone (25 g.), morpholinium chloride (22 g.), and paraformaldehyde (8 g.) in ethanol (35 ml.) was boiled (2 hr.). Addition of ether precipitated 2-*morpholinomethyltetral*-1-*one hydrochloride* (39 g.), prisms (from ethanol), m. p. 153—154° (Found: C, 63·9; H, 7·1. $C_{15}H_{20}O_2NCl$ requires C, 64·0; H, 7·2%). The hydrochloride (42 g.) was treated with 4N-sodium hydroxide (150 ml.) saturated with potassium chloride. Extraction with ether and evaporation of the solvent afforded the free base which with acetone (50 ml.) and methyl iodide yielded the *methiodide* (37 g.), plates (from aqueous ethanol), m. p. 200—202° (Found: C, 49·9; H, 5·8. $C_{16}H_{22}O_2NI$ requires C, 49·8; H, 5·5%). A solution of the methiodide (10 g.) and ethyl acetoacetate (3·5 g.) in ethanol (50 ml.) containing sodium ethoxide (from 1·25 g. of sodium) was boiled for 3 hr. and then poured into water (150 ml.) containing acetic acid (3 ml.). Extraction with ether, evaporation of the solvent, and distillation at 180—190°/0·1 mm. gave a syrup which eventually partially crystallised. Separation of the solid and crystallisation from light petroleum gave 1,2,3,9,10,10a-*hexahydro*-3-*oxophenanthrene*, needles (0·5 g.), m. p. 80—81° (Found: C, 84·1; H, 7·2. $C_{14}H_{14}O$ requires C, 84·8; H, 7·1%); $\lambda_{max.}$ 228 and 297 mμ (log ε 4·04 and 4·33) in ethanol, ν 1660 cm.$^{-1}$. The 2,4-*dinitrophenylhydrazone* formed red prisms, m. p. 234—236° (Found: C, 63·8; H, 4·9; N, 14·4. $C_{20}H_{18}O_4N_4$ requires C, 63·5; H, 4·8; N, 14·8%). The ketone (3·5 g.) in ether (20 ml.) was added to phenylmagnesium bromide (from 4·5 g. of bromobenzene) in ether (20 ml.) and the mixture boiled (15 min.). The solution was poured onto ice and 2N-sulphuric acid; the ethereal layer on evaporation gave a syrup (3·9 g.) which was heated with sulphur (1·1 g.) at 220° for 2 hr. The residue in benzene–light petroleum was chromatographed on alumina (200 g.); elution with

[17] Bachmann and Wilds, *J. Amer. Chem. Soc.*, 1938, **60**, 624.

light petroleum–benzene gave **3-*phenylphenanthrene***, m. p. 73° (Found: C, 94·3; H, 5·3. $C_{20}H_{14}$ requires C, 94·5; H, 5·5%); $\lambda_{max.}$ 261 and 302 mμ (log ε 4·74 and 4·30), after purification through the *dipicrate*, m. p. 120—121° (Found: C, 56·0; H, 2·9; N, 11·5. $C_{32}H_{20}O_{12}N_6$ requires C, 56·1; H, 2·9; N, 12·3%). Oxidation of the hydrocarbon with chromium trioxide and acetic acid gave the *quinone*, orange needles (from acetic acid), m. p. 210° (Found: C, 84·7; H, 4·5. $C_{20}H_{12}O_2$ requires C, 84·5; H, 4·3%); $\lambda_{max.}$ 268, 293, and 368 mμ (log ε 4·54, 4·16, and 3·99) in chloroform, which with *o*-phenylenediamine yielded the *quinoxaline*, pale yellow needles (from benzene–light petroleum), m. p. 227—228° (Found: C, 87·1; H, 4·7; N, 7·1. $C_{26}H_{16}N_2$ requires C, 87·8; H, 4·5; N, 7·9%); $\lambda_{max.}$ 262, 285, 303, 316, 379, and 399 mμ (log ε 4·80, 4·73, 4·42, 4·36, 4·29, and 4·37) in ethanol.

m-*Terphenyl.*—3,5-Diphenylcyclohex-2-en-1-one, $\lambda_{max.}$ 285 mμ (log ε 4·27), $\lambda_{min.}$ 245 mμ (log ε 3·51) [**2,4-*dinitrophenylhydrazone***, red needles (from acetic acid), m. p. 223° (Found: N, 12·8. $C_{24}H_{20}O_4N_4$ requires N, 13·1%), and ***hydrazone***, needles (from ethanol), m. p. 163° (Found: C, 81·3; H, 6·8. $C_{18}H_{18}N_2$ requires C, 82·4; H, 6·9%)], was reduced at room temperature by hydrogen (40 lb./sq. in.) to 3,5-diphenylcyclohexanol, needles (from light petroleum), m. p. 111° (lit.,[10] m. p. 127°) (Found: C, 85·4; H, 8·0. Calc. for $C_{18}H_{20}O$: C, 85·7; H, 8·0%), absorbing at 3260 cm.$^{-1}$ (OH with strong hydrogen bonding). This was oxidised by chromic acid and acetic acid to the diphenylcyclohexanone, m. p. 140°, (lit.,[10] m. p. 139—140°) and yielded *m*-terphenyl when dehydrated by phosphoric oxide in boiling xylene, and the xylene layer heated with chloranil. *m*-Terphenyl was advantageously prepared by boiling the diphenylcyclohexenone (5·6 g.) in ether (100 ml.) and benzene (20 ml.) for 10 min. with lithium aluminium hydride (1 g.) in ether (90 ml.). Ammonium chloride solution was added; the ether layer on evaporation yielded an oil (4·4 g.) which was heated with sulphur (1 g.) at 220° for 3 hr. The residue in light petroleum was chromatographed on alumina (200 g.); elution with the same solvent afforded *m*-terphenyl (3·3 g.), m. p. 86°, $\lambda_{max.}$ 247 mμ (log ε 4·60), identical with a sample kindly supplied by Professor D. H. Hey, F.R.S.

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802. *Complex Halides of the Transition Metals. Part I. Tetrahedral Nickel Complexes.*

By Naida S. Gill and R. S. Nyholm.

The factors likely to favour the formation of tetrahedral complex halides of bivalent transition metals are discussed. The preparation of a series of complex halides of the type $R_2[M^{II}Hal_4]$, where R = $[Et_4N]^+$ or $[Ph_3MeAs]^+$, M^{II} = Mn, Fe, Co, Ni, Cu, Zn, and Hal = Cl, Br, I, is reported. The conductivity, spectra, magnetic susceptibility, and crystal structure of the Ni^{II} complexes have been studied and it is concluded that in these compounds the nickel atom is tetrahedrally co-ordinated. Relevant properties of the tetrahalogeno-complexes of Mn^{II}, Co^{II}, Cu^{II}, and Zn^{II} are reported.

As part of a systematic investigation of complex anionic metal halides we have been studying the compounds formed by the bivalent metals Cr^{II}, Mn^{II}, Fe^{II}, Co^{II}, Ni^{II}, Cu^{II}, and Zn^{II}, using as cations large organic groups such as the tetraethylammonium and triphenylmethylarsonium ions. These are convenient as precipitants, partly because they form stable compounds and partly because they confer upon the products solubility in polar organic solvents such as nitromethane and nitrobenzene. We here outline the project and discuss the tetrahalogeno-nickel complexes in detail. Later papers will deal with Fe^{II}, Cr^{II}, and tervalent metals.

If one uses simple crystal-field theory as a guide (with a purely ionic model) one concludes[1] that, in the first Long Period, tetrahedral spin-free complex halides of the type $[M^{II}Hal_4]^{2-}$ are most likely to occur with the non-bonding configurations, d^0, d_γ^2,

[1] Griffith and Orgel, *Quart. Rev.*, 1957, **11**, 381; see also Gillespie and Nyholm, *ibid.*, p. 339.

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$d_\gamma^3 d_\epsilon^3$, $d_\gamma^4 d_\epsilon^3$, and d^{10}. These are exemplified severally by Ca^{II}, Ti^{II}, Mn^{II}, Co^{II}, and Zn^{II}. (A tetrahedral arrangement is also favoured for spin-paired d_γ^4 complexes, *e.g.*, $[ReCl_4]^-$.) However, this theory does not take into account effects such as charge transfer due to covalent bonding or steric hindrance which, as we shall see, can lead to shapes different from those expected on the purely electrostatic model. Evidence for the existence of tetrahedral halogeno-complexes of Ca^{II} (d^0) or Ti^{II} (d^2) is lacking but recently [2] some tetrahedral d_γ^2 complexes of V^{III}, *e.g.*, $[Et_4N][VCl_4]^-$, have been prepared. A number of complexes of Mn^{II} (d^5) believed to contain the $[Mn^{II}Hal_4]^{2-}$ ion have been described, and Jørgensen [3] has recently examined the spectrum of the compound $[Et_4N]_2[MnBr_4]$, considering that this consistent with a tetrahedral anion. The well-known tetrahedral Co^{II} (d^7) complexes are usually blue, in contrast with the octahedral complexes which are generally pink or violet. For reasons discussed later, however, colour is not a very reliable guide to stereochemistry for Co^{II} complexes. The magnetic moment of spin-free Co^{II} complexes also bears a relation to stereochemistry [4] (see p. 4002). The tetrahedral structure of the blue $[CoCl_4]^{2-}$ has been established by *X*-rays in compounds such as Cs_3CoCl_5 and Cs_2CoCl_4.[5,6] There is also good evidence from *X*-rays for the existence of tetrahedral $Zn^{II}(d^{10})$ complexes, *e.g.*, the compound $Cs_2[ZnCl_4]$.[7]

This leaves us with d^3 (V^{II}), d^4 (Cr^{II}), d^6 (Fe^{II}), d^8 (Ni^{II}), and d^9 (Cu^{II}), there being no bivalent d^1 (Sc^{II}) compounds known. Crystal-field theory predicts that for spin-free d^4 and d^9 complexes, Cr^{II} and Cu^{II} respectively, a square planar quadricovalent or tetragonal sexicovalent arrangement is likely. The tetragonal arrangement has been reported in a large number of compounds of bivalent copper and the explanation of this in terms of the Jahn–Teller effect has been discussed by Orgel and Dunitz.[8] Helmholtz and Kruh [9] have, however, reported that the $[CuCl_4]^{2-}$ ion in crystalline Cs_2CuCl_4 is intermediate between a square planar and a tetrahedral shape (see p. 4002). In the cases of V^{II}, Fe^{II}, and Ni^{II} a tetrahedral arrangement involves the electronic configurations $d_\gamma^2 d_\epsilon^1$, $d_\gamma^4 d_\epsilon^2$, and $d_\gamma^4 d_\epsilon^4$ respectively for the ground state. Even allowing for some mixing-in of upper states, one might expect the unsymmetrical d_ϵ sub-shell in each of these ions to cause some distortion from a regular tetrahedral structure; calculations of the crystal-field stabilisation energy suggest that the octahedron is likely to be the more stable structure,[10] but see below.

Until recently, definite proof that Ni^{II} was ever tetrahedrally co-ordinated was lacking. Indeed, the apparent non-existence of tetrahedral Ni^{II} complexes was generally assumed to be in accord with simple crystal-field theory.[11] The paramagnetic compound $Ni(NO_3)_2,2Et_3P$ appeared likely to be tetrahedral unless one postulated that the NO_3 group acted as a chelate, but no paramagnetic Ni^{II} compounds were known even to be quadricovalent with certainty. Venanzi and Powell [12] have, however, reported recently that complexes of the type $NiHal_2,2Ph_3P$, which are monomeric, are tetrahedral after studying these by *X*-ray crystallography. They find that there is distortion from a perfect tetrahedron.

The presence of $[NiCl_4]^{2-}$ ions in aqueous solution had been suggested by several workers but this had not been proved definitely.[13] Colour changes in melts of nickel chloride with alkali halides have been taken to indicate complex formation although the identity of the

[2] Scaife, 1959, unpublished work.
[3] Jørgensen, *Acta Chem. Scand.*, 1957, **11**, 53.
[4] Figgis and Nyholm, *J.*, 1954, 12.
[5] Powell and Wells, *J.*, 1935, 359.
[6] Porai-Koshits, *Kristallografiya*, 1956, **1**, 291.
[7] Brehler, *Z. Krist.*, 1957, **109**, 68.
[8] Orgel and Dunitz, *Nature*, 1957, **179**, 462.
[9] Helmholtz and Kruh, *J. Amer. Chem. Soc.*, 1952, **74**, 1176.
[10] See Orgel, Proceedings of the Xth Solvay Congress, Brussels, 1956, p. 308, and Jørgensen, *ibid.*, p. 355, for a discussion of this subject.
[11] Bjerrum and Jørgensen, *Rec. Trav. chim.*, 1956, **75**, 658.
[12] Venanzi, *J.*, 1958, 719; Powell and Venanzi, *Proc. Chem. Soc.*, 1956, 6.
[13] Kiseleva and Kodeeva, *Trudy Moskov. Khim. Technol. Inst. un D.I. Mendeleeva*, 1956, **22**, 89; *Chem. Abs.*, 1957, **51**, 16183; Katzin, *Nature*, 1958, **182**, 1013.

complex was not definitely established.[14] Also, it had been reported that a red colour is observed when nickel iodide and sodium iodide are dissolved in acetone.[15] This is apparently due to the presence of some $[NiI_4]^{2-}$ ion. In 1944, Remy and Meyer[16] noted that a blue colour was produced when $CsNiCl_3$ was melted with excess of cæsium chloride. We have now found that the compound Cs_2NiCl_4 appears to be formed when equimolecular

TABLE 1. *Properties of tetrahalogeno-complexes.*

Compound	Colour in solid state	$\mu_{eff.}$ at 20° c. (B.M.)	Molar conductivity in $MeNO_2$ at 20° (c = 0·0005M)	Molar conductivity in $PhNO_2$ at 25° (c = 0·0005M)
$[Ph_3MeAs]_2[NiCl_4]$	Blue	3·89	173	56
$[Et_4N]_2[NiCl_4]$	Blue	3·87	—	Insol.
$[Et_4N]_2[NiBr_4]$	Blue	3·79	179 (0·0008M)	Insol.
$[Ph_3MeAs]_2[NiI_4]$	Red	3·49	163	53
$[Ph_3MeAs]_2[CoCl_4]$	Blue	4·69	173	55
$[Ph_3MeAs]_2[CoBr_4]$	Blue	4·74	162	54
$[Ph_3MeAs]_2[CoI_4]$	Green	4·85	151	53
$[Ph_3MeAs]_2[MnCl_4]$	Pale green	5·88	188	57
$[Et_4N]_2[MnCl_4]$	Pale green	5·94	200	Insol.
$[Ph_3MeAs]_2[MnBr_4]$ ...	Yellow-green	5·87	179	—
$[Et_4N]_2[MnBr_4]$	Yellow-green	5·97	197	Insol.
$[Ph_3MeAs]_2[MnI_4]$	Pale yellow	5·87	—	—
$[Ph_3MeAs]_2[ZnCl_4]$ ...	White	Diamag. ($-0·56 \times 10^{-6}$)	174	53
$[Ph_3MeAs]_2[ZnBr_4]$ ...	White	Diamag. ($-0·50 \times 10^{-6}$)	165	—
$Ph_3MeAs]_2[ZnI_4]$	White	Diamag. ($-0·44 \times 10^{-6}$)	153	—
$[Ph_3MeAs]_2[CuCl_4]$ ...	Yellow	1·91	171	60
$[Ph_3MeAs]_2[CuBr_4]$ ...	Purple	1·96	172	—
Reference compounds for conductivities:				
$[Ph_3MeAs]I$			85	—
$[Et_4N]I$	(1 : 1 Electrolyte)		97	—
$[Co(diars)_2][ClO_4]_2$	(2 : 1 Electrolyte)		177	55 (0·00002M)
$[Co(diars)_3][ClO_4]_3$	(3 : 1 Electrolyte)		262	92 (0·00002M)

proportions of these compounds are melted together, but the complex is stable at high temperatures only; it reverts to the starting materials when cooled below about 70°. More recently, Jørgensen[17] deduced the expected positions of the absorption bands due to $[NiCl_4]^{2-}$ in melts containing $NiCl_2$ by allowing for the absorption due to the (suggested) $[NiCl_6]^{4-}$ ion.

By using alcohol as a solvent we have been able to isolate stable salts of the $Ni[Hal_4]^{2-}$ ion without difficulty. The tetraethylammonium and triphenylmethylarsonium cations are suitable; the properties of the complex chlorides, bromides, and iodides are given in Table 1, together with the corresponding data for certain similar complexes of Mn^{II}, Co^{II}, Cu^{II}, and Zn^{II}. It has not been found possible to isolate all tetrahalogeno-complexes of *both* cations, *e.g.*, neither the $[Ph_3MeAs]_2[NiBr_4]$ complex nor the $[Et_4N]_2NiI_4$ compound was obtained pure. It appears that whether one can isolate a particular $M_2^I[M^{II}Cl_4]$ complex depends on the relative stability of the complex anion and the lattice energy of the precipitated salt, the latter being dependent on relative sizes of ions.

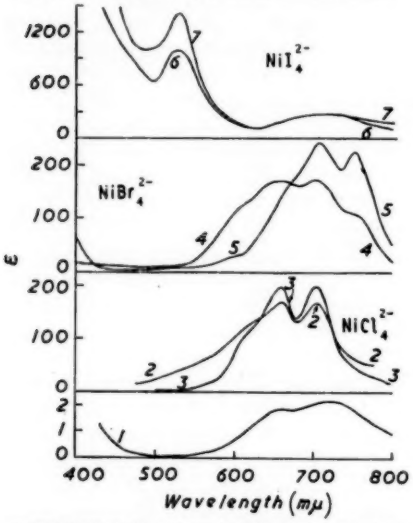
The conductivity data indicate that all compounds are uni-bivalent electrolytes in the solvents used. Unfortunately, molecular-weight studies by freezing-point depression were not feasible owing to the low solubilities in nitrobenzene and other suitable solvents.

The colours of the quadricovalent nickel complexes are much more intense than those of the corresponding octahedral hexa-aquonickel(II) compounds. This has also been

[14] Gruen, *J. Inorg. Nuclear Chem.*, 1957, **4**, 74; Boston and Smith, *J. Phys. Chem.*, 1958, **62**, 409.
[15] Cambi, *Gazzetta*, 1909, **39**, 361.
[16] Remy and Meyer, *Ber.*, 1944, **77**, 679.
[17] Jørgensen, *Molec. Phys.*, 1958, **1**, 410.

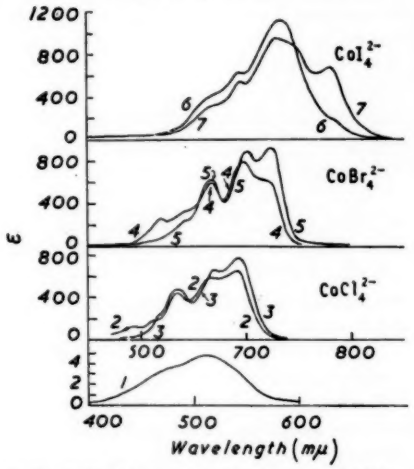
observed in the case of Co^{II} complexes, the blue $[CoCl_4]^{2-}$ ion having an intensity of colour * about 100 times that of the pink $[Co(H_2O)_6]_2^{+}$ ion. This intensity effect has led to some confusion when workers have attempted to correlate the stereochemistry of Co^{II} complexes with the colour. Thus, the pink colour of a hexa-aquocobalt(II) solution changes to blue when as little as 2% of the complex has been changed to the tetrahedral form. The spectra of the various halogenonickel(II) complexes in nitromethane are given in Fig. 1

FIG. 1. *Absorption spectra in nitromethane.*



(1) $Ni(H_2O)_6^{2+}$ in water; (2) $[NiCl_4]^{2-}$, 0·0005M; (3) $[NiCl_4]^{2-}$, 0·0006M, with added Cl^-; (4) $[NiBr_4]^{2-}$, 0·0007M; (5) $[NiBr_4]^{2-}$, 0·0008M, with added Br^-; (6) $[NiI^4]^{2-}$, 0·00025M; (7) $[NiI_4]^{2-}$, 0·00025M, with added I^-.

FIG. 2. *Absorption spectra in nitromethane.*



(1) $Co(H_2O)_6^{2+}$ in water; (2) $[CoCl_4]^{2-}$, 0·0005M; (3) $[CoCl_4]^{2-}$, 0·0005M, with added Cl^-; (4) $[CoBr_4]^{2-}$, 0·0005M; (5) $[CoBr_4]^{2-}$, 0·0005M, with added Br^-; (6) $[CoI_4]^{2-}$, 0·0005M; (7) $[CoI_4]^{2-}$, 0·0005M, with added I^-.

together with the spectrum of the $[Ni(H_2O)_6]^{2+}$ ion. In Fig. 2 the spectra of the corresponding cobalt compounds are recorded for comparison.

The cobalt spectra, measured in the presence of excess of halide ions, have ε values considerably higher than previously reported; these are discussed below. Values of $\lambda_{max.}$ and ε for all complexes of Mn^{II}, Co^{II}, Ni^{II}, and Co^{II} are given in Table 2. A solution of $[Et_4N]_2NiCl_4$ on standing in nitromethane slowly became cloudy with deposition of a little anhydrous nickel chloride. Before opalescence develops an $\varepsilon_{max.}$ of 170 at 660 and 700 mμ is observed; addition of $[Et_4N]Cl$ increases the value of $\varepsilon_{max.}$ to 200 but there is no change in the *position* of the maxima. This suggests an equilibrium of the type, $[NiCl_4]^{2-} \rightleftharpoons NiCl_{2(c)} + 2Cl^-$ which is reversed by the addition of chloride ions. Since there is no change in the position of the band on addition of chloride ions in the large excess necessary to obtain a constant value of ε, it is not considered that any significant concentration of $[NiCl_6]^{4-}$ is formed. The same effect of an increased ε with $CoCl_4^{2-}$ and $CoBr_4^{2-}$ is also observed (see Fig. 2).

The frequencies and values of the extinction coefficients of these bands call for comment, especially in relation to those observed for octahedral complexes. Three types of band are observed in the spectra of octahedral transition-metal complexes.[10,18] First, charge-transfer bands, having large $\varepsilon_{max.}$ values (1000—10,000); these usually occur in the 200—400 mμ region but may overlap the visible region. Secondly, Laporte-forbidden *d–d* bands

* As estimated from the extinction coefficient only.

[18] Orgel, *J. Chem. Phys.*, 1955, **23**, 1004.

which are observed in the visible, near-ultraviolet, and near-infrared regions for octahedral complexes and have $\varepsilon_{max.}$ values in the range 1—10. Thirdly, bands which are *both* Laporte- *and* spin-forbidden which are observed in the case of spin-free d^5 complexes (*e.g.*, Mn^{II}), these have much smaller $\varepsilon_{max.}$ values (*ca.* 0·01).

In the octahedral hexa-aquo-bivalent-metal complexes the d_ϵ–d_γ separation (Δ) is about 8000—13,000 cm.$^{-1}$. The value estimated for $[Ni(H_2O)_6]^{2+}$ being 8500 cm.$^{-1}$, the band observed at 723 mμ has been assigned to one of the two possible $d_\epsilon^6 d_\gamma^2 \longrightarrow d_\epsilon^5 d_\gamma^3$ transitions. A similar $d_\epsilon^5 d_\gamma^2 \longrightarrow d_\epsilon^4 d_\gamma^3$ band for the $[Co(H_2O)_6]^{2+}$ ion is also shown. In the tetrahedral complexes the d_ϵ and d_γ levels are inverted and the separation between them is less

TABLE 2. *Spectra of tetrahalogeno-complexes in visible region.*

Complex ion	$\varepsilon_{max.}$	$\lambda_{max.}$	Ref.	Concn. of $CH_3{\cdot}NO_2$ soln. (M)	Complex ion	$\varepsilon_{max.}$	$\lambda_{max.}$	Ref.	Concn. of $CH_3{\cdot}NO_2$ soln. (M)
$[Co(H_2O)_6]^{2+}$ ...	4·8	513	*c*, *d*		$[Ni(H_2O)_6]^{2+}$	2·2	723	*b*, *c*, *d*	
	(sh.)	454				2·0	663		
$[CoCl_4]^{2-}$	653	693	*a*, *b*, *h*	0·0005		5·1	395		
	580	668			$[NiCl_4]^{2-}$	167	700	*b*	0·005
	419	635				167	660		
	(sh.)	613				(sh.)	610		
	122	593			$[NiBr_4]^{2-}$ ...	(sh.)	750	*b*	0·0008
$[CoBr_4]^{2-}$	(sh.)	723	*b*, *h*	0·0005		173	698		
	790	698				168	652		
	595	668				(sh.)	608		
	332	645			$[NiI_4]^{2-}$	278	~725 *	*b*	0·00025
	254	618				1096	530		
$[CoI_4]^{2-}$	(sh.)	783	*b*, *h*	0·0005	$[Mn(H_2O)_6]^{2+}$	0·017	532	*c*, *f*	
	1126	733				0·014	435		
	634	693				0·036	402		
	(sh.)	663				(sh.)	397		
$[Cu(H_2O)_6]^{2+}$ ...	13	~800 *	*c*, *e*			0·023	357		
$CuCl_4]^{2-}$	88	~890 *	*b*, *g*	0·0005		0·021	337		
	(sh.)	435			$[MnCl_4]^{2-}$ ...	0·71	445	*b*	0·1
	~4000	360				0·47	430		
$[CuBr_4]^{2-}$	122	~870 *	*b*	0·0005	$[MnBr_4]^{2-}$ ...	(sh.)	465	*b*	0·05
	1774	643				1·91	452		
	1995	433				1·00	437		
	~3000	369				2·37	371		

* = Broad.

[a] Ballhausen and Jørgensen, *Acta Chem. Scand.*, 1955, **9**, 397. [b] This work. [c] Orgel, *J. Chem. Phys.*, 1955, **23**, 1004. [d] Jørgensen, *Acta Chem. Scand.*, 1954, **8**, 1495. [e] Bjerrum, Ballhausen, and Jørgensen, *Acta Chem. Scand.*, 1954, **8**, 1275. [f] Jørgensen, *Acta Chem. Scand.*, 1954, **8**, 1502. [g] Helmholtz and Kruh, *J. Amer. Chem. Soc.*, 1952, **74**, 1176. [h] Jørgensen, *Acta Chem. Scand.*, 1957, **11**, 53.

than half (theoretically 4/9) of the value of Δ for an octahedral complex. The single-electron transitions between d_ϵ and d_γ levels then occur at much longer wavelengths. In the case of tetrahedral cobalt complexes the two transitions from the singlet ($^4A_2$) ground state to the first ($^4T_1$) and second ($^4T_2$) triplet levels of the F state have frequencies in the vicinity of 3000 cm.$^{-1}$ and 5000 cm.$^{-1}$, respectively, well outside the visible region. The band observed for $[CoCl_4]^{2-}$ in the visible region is generally considered [19] to correspond to a transition from the singlet level of the F state ($^4A_2$) to the ^4P state ($^4T_2$). For the $[NiCl_4]^{2-}$ complex the observed band at about 700 mμ is presumably due to a transition from the lowest-lying triplet of the F state ($^3T_1$) to the ^3P state. The position of these bands corresponds fairly closely to those deduced by Jørgensen [17] for $[NiCl_4]^{2-}$ from considerations of spectra of melts of nickel chloride with alkali halides. There is, however, no agreement with the predicted extinction coefficients. In all cases a change from the octahedral hexa-aquo- to the quadri-covalent halogeno-complexes of Mn^{II}, Co^{II}, and Cu^{II} results in at least a 100-fold increase in the extinction coefficient. This is observed also for the $[NiHal_4]^{2-}$ complexes and may be taken as additional support for their formulation

[19] Ballhausen and Liehr, *J. Amer. Chem. Soc.*, 1959, **81**, 538.

as quadri-covalent halogeno-complexes in solution. Scaife [2] has observed a similar increase in passing from the $[V(H_2O)_6]^{3+}$ to the $[VCl_4]^-$ ion.

The reason for the high intensity of the $[CoHal_4]^{2-}$ bands is not fully understood. A commonly accepted explanation is that the presence of $4p$ orbitals having the same symmetry as the d_ϵ orbitals enhances the intensity. However, the transition from the A_2 level, arising from the ion F term, to the T_2 level arising from the ion P term, is not Laporte-forbidden and hence in this instance a considerable intensity can be expected. It has also been suggested that the intensity may arise partly from a charge-transfer contribution. It is noteworthy that the complexes of the iodide ion (the most readily polarised ion) have the largest $\epsilon_{max.}$ values of the three halogens; however, the ratio of intensities $[CoCl_4]^{2-}$: $[CoI_4]^{2-}$ is still only about 2 : 1. Charge-transfer effects would make it easier to understand the large ϵ values for the $[CuCl_4]^{2-}$ and $[CuBr_4]^{2-}$ ions in nitromethane, in which solvent a tetrahedral arrangement is not at all certain. Thus, Helmholtz and Kruh have reported that the $[CuCl_4]^{2-}$ ion in crystalline Cs_2CuCl_4 is an irregular tetrahedron. One expects for a perfect tetraheron a relatively large orbital contribution to the magnetic moment, leading to a $\mu_{eff.}$ of about 2·2 B.M.[20] We find a value of 1·96, in agreement with Figgis and Harris [21] who report 2·0 B.M. For the $[Ph_3MeAs]_2CuCl_4$ complex we obtained a value of 1·91 B.M. These values support the view that there is marked deviation from any regular tetrahedral arrangement in the solid state. We find, moreover, that $\mu_{eff.}$ for $[Ph_3MeAs]_2CuCl_4$ in nitromethane solutions is 1·95 B.M. Although in this solvent one might expect to minimise forces between the complex ions and hence to favour the formation of a regular tetrahedron as suggested by Ballhausen and Liehr,[19] the low moment obtained certainly does not support the postulated regular tetrahedral arrangement. A more detailed discussion of these spectra will be published shortly by Dr. T. M. Dunn.

[Note added in proof: Gruen and McBeth (*J. Phys. Chem.*, 1959, **63**, 393) have recently published the spectrum of $[NiCl_4]^{2-}$ in a melt made from nickel chloride and pyridinium chloride and this agrees closely with our Fig. 1.]

On the question of the stereochemistry of the nickel complexes the magnetic data are specially significant (see Table 1). Since the stereochemistry of the attached ligands affects the quenching of orbital magnetism, the size of the latter may in suitable cases be used as a guide to stereochemistry. Thus, octahedral spin-free Co^{II} complexes usually have moments in the region 4·8—5·2 B.M., whereas the moments of tetrahedral complexes are usually considerably less (4·3—4·8 B.M.) (see however, $[CoI_4]^{2-}$ p. 3999). For octahedral Co^{II} complexes the lowest-lying level of the F state is a triplet, hence a large orbital contribution in excess of the spin-only moment of 3·88 B.M. is expected. For tetrahedral Co^{II} complexes the lowest-lying level is a singlet, but the moment still exceeds 3·88 B.M. because spin-orbit coupling can " mix in " some of the first (and even second) excited state, which is a triplet, since this is only about 3000 cm.$^{-1}$ higher in energy. This separation Δ becomes gradually smaller in the sequence $[CoCl_4]^{2-} > [CoBr_4]^{2-} > [CoI_4]^{2-}$, which explains the steadily increasing moments obtained along this series (see Table 1). Similar results have been obtained by Cotton.[22] Thus in this instance the moment alone is not a safe guide to stereochemistry.

The moments of the tetrahalogeno-nickel complexes (3·6—4·0 B.M.) are much higher than those observed for octahedral Ni^{II} complexes (2·9—3·2 B.M.), and especially so in the case of the tetrachloro-ion. This is what one would expect for a bivalent nickel atom surrounded by a perfect tetrahedron of negative charges; the situation is opposite to that obtaining with bivalent cobalt, an orbital triplet lying lowest in $[NiCl_4]^{2-}$. In Table 3 are shown the $\mu_{eff.}$ values calculated for various circumstances. The moment of the $[NiCl_4]^{2-}$ complex has been measured over a temperature range (−178° to +25°) and this gives a θ value of approximately 35°; the $\mu_{eff.}$ calculated by using this value of θ is 4·1$_2$ B.M. Fig.

[20] Figgis, *Nature*, 1958, **182**, 1568.
[21] Figgis and Harris, *J.*, 1959, 855.
[22] Cotton, 1959, personal communication.

3 shows the plot of susceptibility against temperature. The moment in solution in nitromethane is 4·0 B.M., a little larger than in the solid but the difference is not significant for this discussion. The moment does show, however, that the $[NiCl_4]^{2-}$ ion does not distort in this solvent so as to remove the degeneracy and hence that the presumed tetrahedral arrangement still obtains in solution.

The interpretation of the order of the moments ($[NiCl_4]^{2-} > [NiBr_4]^{2-} > [NiI_4]^{2-}$) is not as straightforward as in the corresponding tetrahalogenocobalt(II) complexes. In

TABLE 3. *Predicted magnetic moments for spin-free bivalent nickel complexes.*

No.	Environment of Ni^{II} atom	$\mu_{eff.}$ (B.M.) (calc.)
1	Free Ni^{2+} ion ($^3F_4$). No electrical field. $S = 1$, $L = 3$. Assume $\lambda = 0$	4·47 *
2	As in (1) but assuming usual value of λ (~ -335 cm.$^{-1}$)	5·56
3	As in (1) but assuming $\lambda = \infty$	5·59 †
4	Ni^{2+} ion in perfect octahedral field of negative charges; assume $\lambda = 0$	2·83
5	Octahedral Ni^{II}, *e.g.*, $[Ni(H_2O)_6]^{2+}$, using accepted value of λ (varies from ~200 to 324)	~3·1—3·2
6	Ni^{2+} in tetrahedral field of negative charges assuming $\lambda = 0$ and large value of Δ (assume $L = 1$)	3·16 *
7	As in (6) but using same value of λ as in octahedral case and assuming Δ is very large, *i.e.*, only configuration to be considered is $d_\gamma^4 d_\epsilon^4$	~3·6
8	As in (7) but with Δ small enough to permit configuration interaction (*i.e.*, weak field). Moment can be as large as 4·1	~4·1

λ = Spin–orbit coupling constant.
* Using $\mu = \sqrt{[4S(S+1) + L(L+1)]}$. † Using $\mu = g\sqrt{[J(J+1)]}$.

tetrahedral Ni^{II} both the lowest level and the first excited level are orbital triplets; " mixing-in " of the latter by spin–orbit coupling is not expected to lead to a reduction in moment. However, the moment could be reduced by mixing-in some of the second excited state since this is a singlet. By analogy with $[CoCl_4]^{2-}$ this level is presumed to be about 6000 cm.$^{-1}$ above the ground state, and the separation (Δ') is expected to decrease in the sequence $[NiCl_4]^{2-} > [NiBr_4]^{2-} > [NiI_4]^{2-}$; hence a greater singlet contribution which is proportional to Δ', is expected as we pass along Cl ⟶ Br ⟶ I with a consequent reduction in moment, as observed. The spin–orbit interaction will increase in the sequence Cl < Br < I, and this also will reduce the moment, the decrease being greatest for the iodide and least for the chloride. There will, of course, be a contribution from the $^3T_2$ level arising from the ^3P free-ion term in each case, but this is not expected to be of such a size as to be of major importance in deciding the *order* of the moments of these ions.

Finally, the appreciably large and positive value of θ calls for comment. This suggests at first sight the possibility of some antiferromagnetic interaction, but alternatively the explanation could be the same as that proposed by Figgis and Lewis [23] for octahedral V^{III} complexes. They suggest that there is an appreciable temperature-independent paramagnetism arising from a splitting of the lowest-lying triplet. We propose to study the susceptibility of a number of these complexes over a range of temperature to throw more light on this problem.

It is noteworthy that tetrahedral complexes of the type $NiX_2,2Ph_3P$ do not have a large orbital contribution, moments of the order 2·9—3·1 B.M. being reported. However, in these compounds there are two different kinds of attached ligand which can provide an asymmetric field, as discussed by Griffith, Lewis, and Wilkinson for $NiNO(OH)_3$.[24] Further, there is in any case appreciable distortion of the tetrahedron which also leads to removal of orbital degeneracy and hence a reduction in the moment closer to the spin-only value. It should be emphasised that the absence of a large orbital contribution does not prove that a Ni^{II} complex is octahedral, but the *presence* of a large orbital moment can be taken as highly suggestive of a tetrahedral arrangement.

[23] Figgis and Lewis, 1959, personal communication.
[24] Griffith, Lewis, and Wilkinson, *J.*, 1959, 1775.

XUM

The conclusion that these complex $[NiHal_4]^{2-}$ ions are tetrahedral is supported by *X*-ray studies carried out by Mr. Peter Pauling.[25] These will be reported later by him in detail. The arsonium salts of $MnCl_4^{2-}$, $MnBr_4^{2-}$, $FeCl_4^{2-}$, $CoCl_4^{2-}$, $CoBr_4^{2-}$, $NiCl_4^{2-}$, $ZnCl_4^{2-}$, and $ZnBr_4^{2-}$ are isomorphous, forming cubic crystals with cell edge 15·5 Å (Ni), space-group $P2_1/3$ with four molecules in the unit cell. If it be accepted that $[CoCl_4]^{2-}$ is tetrahedral in the above compound, then it follows that all these complex ions have this arrangement, although very slight distortions are not ruled out. Further, the crystal symmetry is such that the metal atom lies on a three-fold axis, and taken in conjunction with the results of other physicochemical measurements leads to the conclusion that, *if* there is any slight distortion at all, it is in the sense of there being three equivalent halide ions and one non-equivalent ion also on the three-fold axis; this is also in agreement with the deductions from consideration of the spectrum of $[NiCl_4]^{2-}$.[26] Work is in progress on the complete elucidation of the structure of $[Ph_3MeAs]_2[NiCl_4]$. *X*-Ray studies on single crystals also show that the arsonium salts of MnI_4^{2-}, CoI_4^{2-}, NiI_4^{2-}, and ZnI_4^{2-} are isomorphous with one another but not with the tetrabromo- or tetrachloro-compounds. Undoubtedly these too contain tetrahedral complex ions, the change in crystal type being due to the larger size of the I^- ion.

The fact that it is possible to obtain tetrahedral complexes of Ni^{II} and Fe^{II} (to be described in Part II) shows that factors other than the ligand-field effects are important in determining the stereochemistry of complex ions, and in some cases can be of greater importance. The first of these is considered to be the effect of covalent bonding. When an easily polarised ligand is used, the charge transfer per bond from the ligand to the bivalent metal ion must become appreciable. It is considered that this effect plays a major part in deciding the co-ordination number of the metal in accordance with the electroneutrality principle. As pointed out by Pauling,[27] the preferred co-ordination number of a metal atom increases with the valency, and he has suggested that as a rough rule the co-ordination number is twice the valency of the metal atom. However, two or more co-ordination numbers can occur with the same metal ion, *e.g.*, $[FeF_6]^{3-}$ and $[FeCl_4]^-$, $[Co(H_2O)_6]^{2+}$ and $[CoCl_4]^{2-}$. This may be considered to arise, not so much from steric factors as a rule, but from differences in polarisability of the ligands. If it be accepted that charge transfer from F^- to Fe^{3+} in an Fe–F bond is less than from Cl^- to Fe^{3+} in an Fe–Cl bond, then clearly the number of Cl^- ligands needed to effect near electroneutrality of the Fe^{3+} ion is smaller than the number of F^- ligands. However, there is no doubt that steric factors can be of major importance in deciding both co-ordination number and stereochemistry in other cases. If some covalent binding occurs, the most readily available orbitals are $4s4p^3$ which, as with ionic binding, give rise to tetrahedral co-ordination.

Crystal-field stabilisation energies (C.F.S.E.) have often been used to predict the relative stabilities of different stereochemical arrangements. In particular, they have been used to support the view that tetrahedral Ni^{II} complexes are unlikely to be stable; some comment thereon is called for. The C.F.S.E. of an octahedral Ni^{II} complex is $1{\cdot}2\Delta$, where Δ is the separation between the d_ϵ and d_γ levels; hence, for the hexa-aquonickel(II) ion C.F.S.E. is about 28·5 kcal./g.-atom. For a tetrahedral complex the C.F.S.E. is only $0{\cdot}8\Delta'$, where Δ' is the separation between d_ϵ and d_γ levels in a tetrahedral complex. Since $\Delta' = \frac{4}{9}\Delta$, we calculate that the C.F.S.E. for a tetrahedral complex is only about 9 kcal./g.-atom of Ni^{II}. However, this stabilisation energy is small compared with the energy evolved in producing the tetrahedral or octahedral ligand field and, further, other effects due to covalent binding could easily be more important. However, the C.F.S.E. *is* of great importance in considering the relative stabilities of a series of complexes of the *same* kind, *e.g.*, the hexa-aquo-complexes of bivalent metals.

In the light of the above it is of interest to examine the circumstances favouring the

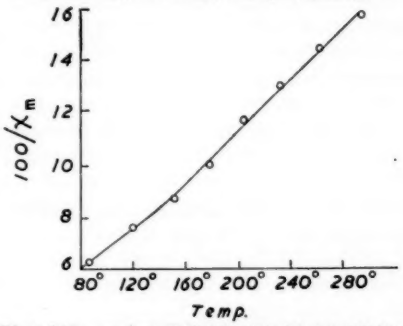
[25] P. Pauling, 1959, personal communication.
[26] T. Dunn, 1959, personal communication.
[27] L. Pauling, *J.*, 1948, 1461.

formation of these tetrahalogeno-complexes, especially in aqueous solution. Consider the reaction

$$[Co(H_2O_6)]^{2+} + 4Cl^- (Solv.) \rightleftharpoons [CoCl_4]^{2-} + 6H_2O$$

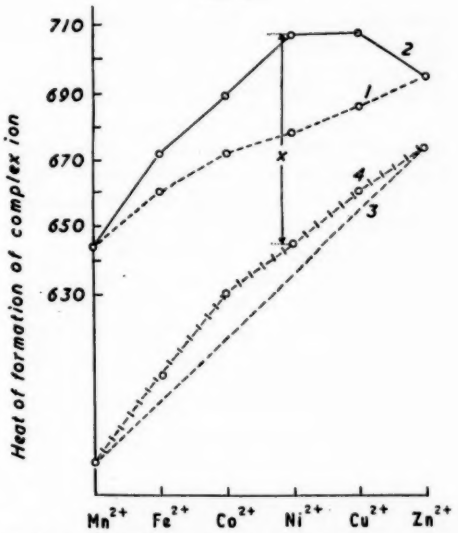
in various solvents. In water the large hydration energy of Cl^- tends to keep the equilibrium well to the left-hand side. To help to force the reaction to the right, one could change to a solvent of smaller solvating power; alcohol is effective in this way. An increase in temperature also moves the equilibrium to the right, presumably owing to a decrease in the solvation of the chloride ion. This is reflected in the marked colour change, usually from green to blue, as the temperature is increased.

FIG. 3. *Magnetic susceptibility of* $[NiCl_4]^{2-}$.



Plot of $1/\chi_m$ against T (°K) for $(Ph_3MeAs)_2[NiCl_4]$.

FIG. 4.



(1) Corrected (C.F.S.E.) heat of hydration of ions $[M(H_2O)_6]^{2+}$. (2) Experimental heat of hydration of ions $[M(H_2O)_6]^{2+}$. (3) Corrected (C.F.S.E.) heat of formation of ions MCl_4^{2-} (hypothetical). (4) Hypothetical heat of formation of ions MCl_4^{2-}.

The problem remaining is to explain why Ni^{II} does not form $NiCl_4^{2-}$ complexes in water whilst both the preceding element (Co^{II}) and the next one (Cu^{II}) do. Fig. 4 suggests an explanation. To obtain this we have used accepted values [10,18] of Δ for octahedral hexa-aquo-complexes and have taken Δ for tetrahedral complexes as $\frac{4}{9}$ of this. Since we will be dealing with the ligand Cl^- rather than H_2O, one ought to take an even larger value. However, as comparative results only are required this seems justifiable. It is known that the *corrected* heats of hydration of the hexa-aquo-bivalent-metal ions increase steadily from Mn^{II} to Cu^{II} and then fall to zinc.[28,10] These are shown in curve (1), which is obtained by subtracting the stabilisation energies from the experimental curve (2). Now let us assume that the corrected heats of formation of $[MCl_4]^{2-}$ fall on the straight line (3). For experimental reasons which emerge shortly we suggest that this curve is steeper than (1). On adding to this the (estimated) stabilisation energies we get curve (4). Now the separation between these two curves (2) and (4) is a ΔH value, but, since it is reasonable to assume that the ΔS value for the reaction $[M(H_2O)_6]^{2+} + 4Cl^-,aq \rightleftharpoons [MCl_4]^{2-} + 6H_2O$ is approximately the same for all metals from Mn to Zn, the separation x can be used as a

[28] Holmes and McClure, *J. Chem. Phys.*, 1957, **26**, 1686.

comparative measure of ΔG. Now if curves (1) and (3) do converge as shown, then by ignoring first any C.F.S.E., a steadily increasing tendency to form $[MCl_4]^{2-}$ complexes as we pass from Mn to Zn can be explained. However, in passing from Co^{II} to Ni^{II} the enhanced tendency to form $[NiCl_4]^{2-}$ due to convergence of curves (1) and (3) must be weighed against the relative differences between the C.F.S.E. values for octa- and tetra-hedral co-ordination. For the various elements concerned these differences are roughly: Mn^{II}, 0; Fe^{II}, $12 - 8 = 4$; Co^{II}, $22 - 14 = 8$; Ni^{II}, $28{\cdot}5 - 8{\cdot}6 = 20$; Cu^{II}, $21 - 6 = 15$; Zn^{II}, 0. Thus the convergence in passing from Co^{II} to Ni^{II} has to be sufficient to outweigh a relative destabilisation of an *extra* 11 kcal. due to C.F.S.E. for Ni^{II} *over and above* the value for cobalt. It is suggested that this quantity causes the instability of $[NiCl_4]^{2-}$ in water relative to $[CoCl_4]^{2-}$. It must be emphasised, however, that this tells us nothing about the actual heat of formation of the $[NiCl_4]^{2-}$ ion which is clearly very stable in the absence of water. Some support for the proposal that curves (3) and (1) are convergent emerges from a study of the curves by Holmes and McClure [28] for the heats of formation of bi- and ter-valent hexahydrates. They show that the curve for ΔH of hydration of the latter is steeper than that for the former. It is suggested that curve (3) for the tetrahalides, like the curve for the tervalent hexahydrates, is steeper than (1) because there is greater covalent character in the metal–ligand bond than there is in the bivalent hydrates. This has been expressed in another way by Williams.[29] He points out that, as we pass across the transition series, *e.g.*, from $Ti^{2+} \longrightarrow Cu^{2+}$, *i.e.*, as the polarising power of the cation increases, the tendency to complex with more easily polarised ligands increases. Thus H_2O is preferred to NH_3 at the beginning of the series but NH_3 to H_2O at the end.

The isolation of these regular tetrahedral $[NiHal_4]^{2-}$ complexes has emphasised the importance of covalent bonding in compounds of this type. It also shows that the tetrahedral arrangement is little affected by the presence of an asymmetric d_ϵ shell (*i.e.*, one which is not empty, half-full, or filled). This is in marked contrast to the well-known distortion which occurs in the sexicovalent complexes where an unsymmetrical d_γ shell causes marked deviation from a regular octahedral arrangement.

Experimental

Preparation.—All compounds were prepared by mixing the calculated amounts of the appropriate metal halide (not necessarily anhydrous) and arsonium or tetraethylammonium halide dissolved in ethyl alcohol. The products were recrystallised from ethyl alcohol except bis-(tetraethylammonium) tetrabromomanganese(II) for which methyl alcohol was used.

Nickel Compounds.—*Bis(triphenylmethylarsonium) tetrachloronickelate*(II), blue hygroscopic needles (Found: C, 53·9; H, 4·4; Cl, 16·6; Ni, 6·9. $C_{38}H_{36}Cl_4As_2Ni$ requires C, 54·1; H, 4·3; Cl, 16·8; Ni, 7·0%). *Bis(tetraethylammonium) tetrachloronickelate*(II), blue deliquescent needles (Found: C, 41·8; H, 8·9; Cl, 30·7; Ni, 12·9. $C_{16}H_{40}N_2Cl_4Ni$ requires C, 41·7; H, 8·7; Cl, 30·8; Ni, 12·7%). *Bis(tetraethylammonium) tetrabromonickelate*(II), blue deliquescent needles (Found: C, 30·1; H, 6·5; N, 4·6; Br, 49·8. $C_{16}H_{40}N_2Br_4Ni$ requires C, 30·1; H, 6·3; N, 4·4; Br, 50·0%). *Bis(triphenylmethylarsonium) tetraiodonickelate*(II), red leaflets from hot ethyl alcohol but dissociated when the mixture was cooled; it was therefore filtered from the mother liquor while still warm; the crystals are hygroscopic (Found: C, 37·1; H, 3·5; I, 42·0. $C_{38}H_{36}I_4As_2Ni$ requires C, 37·75; H, 3·0; I, 42·1%).

Cobalt Compounds.—*Bis(triphenylmethylarsonium) tetrachlorocobaltate*(II), blue needles (Found: C, 54·2; H, 4·7; Cl, 16·6; Co, 6·7. $C_{38}H_{36}Cl_4As_2Co$ requires C, 54·1; H, 4·3; Cl, 16·8; Co, 7·0%). *Bis(triphenylmethylarsonium) tetrabromocobaltate*(II), blue needles (Found: C, 44·4; H, 3·8; Co, 5·5. $C_{38}H_{36}Br_4As_2Co$ requires C, 44·7; H, 3·55; Co, 5·8%). *Bis(triphenylmethylarsonium) tetraiodocobaltate*(II), green leaflets (Found: C, 37·8; H, 3·2. $C_{38}H_{36}I_4As_2Co$ requires C, 37·75; H, 3·0%).

Manganese Compounds.—*Bis(triphenylmethylarsonium) tetrachloromanganate*(II), very pale green, deliquescent needles (Found: C, 53·9; H, 4·5; Cl, 16·6. $C_{38}H_{36}Cl_4As_2Mn$ requires C, 54·4; H, 4·3; Cl, 16·9%). *Bis(tetraethylammonium) tetrachloromanganate*(II), very pale green needles (Found: C, 42·3; H, 8·8; N, 6·5. $C_{16}H_{40}N_2Cl_4Mn$ requires C, 42·0; H, 8·8; N, 6·1%).

[29] Williams, *J. Roy. Inst. Chem.*, 1959, 234.

Bis(triphenylmethylarsonium) tetrabromomanganate(II), pale green, deliquescent needles (Found: C, 44·8; H, 4·0. $C_{38}H_{36}Br_4As_2Mn$ requires C, 44·9; H, 3·6%). *Bis(tetraethylammonium) tetrabromomanganate*(II), pale green needles (Found: C, 30·9; H, 6·2; N, 4·4. $C_{16}H_{40}N_2Br_4Mn$ requires C, 30·2; H, 6·35; N, 4·4%). *Bis(triphenylmethylarsonium) tetraiodomanganate*(II), cream leaflets which when dry slowly decompose and finally become brown owing to formation of iodine (Found: C, 38·1; H, 3·3. $C_{38}H_{36}I_4As_2Mn$ requires C, 37·9; H, 3·0%).

Zinc Compounds.—*Bis(triphenylmethylarsonium) tetrachlorozincate*(II), white needles (Found: C, 53·7; H, 4·5; Cl, 16·4. $C_{38}H_{36}Cl_4As_2Zn$ requires C, 53·7; H, 4·3; Cl, 16·7%). *Bis(triphenylmethylarsonium) tetrabromozincate*(II), white needles (Found: C, 44·3; H, 4·0. $C_{38}H_{36}Br_4As_2Zn$ requires C, 44·4; H, 3·5%). *Bis(triphenylmethylarsonium) tetraiodozincate*(II), white leaflets (Found: C, 38·0; H, 3·5. $C_{38}H_{36}I_4As_2Zn$ requires C, 37·55; H, 3·0%).

Copper Compounds.—*Bis(triphenylmethylarsonium) tetrachlorocuprate*(II), yellow needles (Found: C, 54·0; H, 4·4; Cl, 16·4. $C_{38}H_{36}Cl_4As_2Cu$ requires C, 53·8; H, 4·3; Cl, 16·7%). *Bis(triphenylmethylarsonium) tetrabromocuprate*(II), purple needles (Found: C, 44·3; H, 3·7. $C_{38}H_{36}Br_4As_2Cu$ requires C, 44·5; H, 3·5%).

Absorption spectra were obtained with a Unicam SP.500 spectrophotometer. Magnetic susceptibilities were determined by the Gouy method.[30]

One of us (N. S. G.) acknowledges the award of a Turner and Newall Research Fellowship. We are also grateful to Dr. T. Dunn and Dr. J. Lewis for discussions.

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UNIVERSITY COLLEGE, LONDON. [*Received, May 11th,* 1959.]

[30] Figgis and Nyholm, *J.*, 1959, 331.

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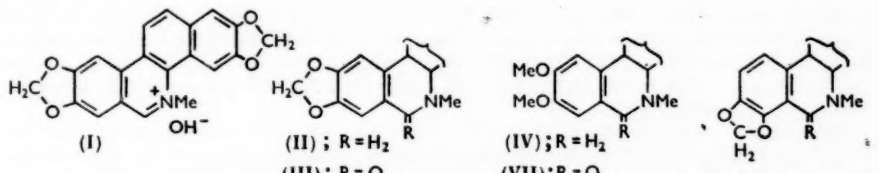
803. *An Examination of the Rutaceae of Hong Kong. Part III.*[1] *The Alkaloid, Avicine, from* Zanthoxylum avicennae.

By H. R. ARTHUR, (MISS) W. H. HUI, and (in part) (MISS) Y. L. NG.

A new benzophenanthridine alkaloid, avicine, has been isolated from the root bark of *Zanthoxylum avicennae*. Avicine is related to nitidine in the same way as sanguinarine is related to chelerythrine. Hesperidin has been obtained from the leaves, and a mixture of hesperidin, diosmin, and, avicennin, from the root bark of this plant.

Zanthoxylum avicennae (Lam.) DC. (*Ying pu po*), an erect shrub with white flower, is used in the Colony against sore throat and jaundice. The bark was earlier reported to contain a mixture of hesperidin and diosmin [2] and a new yellow coumarin, avicennin.[3]

Hesperidin has now been obtained from the leaves, and a mixture of hesperidin, diosmin, and avicennin and also a new benzophenanthridine alkaloid, avicine (I), from the root bark.



Avicine was isolated from the methanol extract as a crude quaternary salt which yielded a mixture of dihydroavicine (II), and oxyavicine (III), when its aqueous solution was basified. (This disproportionation of avicine occurred less readily than that of

[1] Part II, *J.*, 1959, 1840.
[2] Arthur, Hui, and Ma, *J.*, 1956, 632.
[3] Arthur, "Proceedings of the Phytochemical Symposium, Kuala Lumpur," 1957, p. 123.

nitidine [1] isolated from *Zanthoxylum nitidum*.) Like dihydronitidine (IV), dihydroavicine was easily oxidised by air and so it was separated from oxyavicine under argon. The general chemical properties and ultraviolet absorption spectra of these two compounds suggested that they were benzophenanthridine derivatives. Oxyavicine, a substituted amide, did not form salts. It was converted into dihydroavicine by reduction and dihydroavicine was converted into oxyavicine by oxidation *via* the quaternary avicine acetate. Whilst dihydroavicine and oxyavicine were shown not to contain methoxyl groups, a positive Labat test indicated the presence of methylenedioxy-groups; and so it was clear that dihydroavicine was isomeric with, and contained the same functional groups as, dihydrosanguinarine (V) and that oxyavicine was similarly related to oxysanguinarine (VI).

Demethylenation of oxyavicine gave a tetrahydric phenol which on methylation yielded 6,7,2′,3′-tetramethoxy-10-methyl-1,2-benzophenanthridone previously obtained [1] from oxynitidine (VII). Hence it was clear that the methylenedioxy-groups of oxyavicine (and those of avicine and dihydroavicine) were present in the 6,7- and 2′,3′-positions of the benzophenanthridine skeleton; and that avicine is 6,7:2′,3′-bismethylenedioxy-10-methyl-1,2-benzophenanthridium hydroxide. Salts of this alkaloid and of dihydroavicine have been prepared.

Avicine, whose existence might have been predicted on biogenetic grounds particularly following the discovery of nitidine, is related to nitidine as sanguinarine is related to chelerythrine.

There was no evidence that oxyavicine (cf. oxynitidine [1]) occurred in the root bark.

Experimental

Analyses were by Dr. Zimmermann, Melbourne. The alumina used was B.D.H. analysis grade. Unless otherwise stated m. p.s were taken on a Kofler block; where stated to have been taken on a gas-heated copper block the m. p.s are uncorrected.

Isolation of Products.—Leaves (400 g.) were extracted with hot methanol (3 l.) for 20 hr. The extract was concentrated to 100 ml., and left for 2 days. The green solid (0·4 g.) which separated was extracted with light petroleum (b. p. 60—80°) and then with methanol. The pale brown residue was recrystallised twice from aqueous pyridine. Nearly colourless fine needles of hesperidin hydrate, m. p. 260° (decomp.; vac.; gas-heated copper block), were obtained.

Milled root bark (2·5 kg.) was extracted with hot methanol (16 l.) for 30 hr. The extract was concentrated to 1 l., then left for 3 days. The pale yellow crystals *A* (8·0 g.) were collected, and the filtrate concentrated to 0·5 l. and left for 3 more days. The crude bright yellow alkaloid salt *B*, (2·4 g.) was collected and then washed with methanol.

Material *A* (8·0 g.) was boiled with methanol, and from the extract avicennin [3] (1·1 g.), m. p. 141—142° alone or in admixture with an authentic sample, was obtained by recrystallisation. The methanol-insoluble fraction of *A* (investigated by Miss Y. L. Ng) on recrystallisation from aqueous pyridine gave diosmin hydrate, m. p. 275—276° (decomp.; vac.; gas-heated copper block) (Found: C, 53·9; H, 5·8. Calc. for $C_{28}H_{32}O_{15},H_2O$: C, 53·7; H, 5·4%); the aqueous pyridine mother-liquors gave, after concentration under reduced pressure, hesperidin hydrate, m. p. 257—260° (decomp.; vac.; gas-heated copper block) (Found: C, 53·9; H, 5·9. Calc. for $C_{28}H_{34}O_{15},H_2O$: C, 53·5; H, 5·7%); it was purified by recrystallisation from aqueous pyridine.

Separation of Dihydroavicine (II) *and Oxyavicine* (III).—Material *B* (4·8 g.) was boiled with water. After being filtered, the hot aqueous solution was basified with ammonia, and the buff-coloured precipitate (3·0 g.) was dried and then extracted with boiling benzene. The benzene extract was chromatographed on alumina (200 g.) under argon. Elution with benzene gave a product (0·7 g.) which, after recrystallisation from ethanol under argon, yielded colourless prisms of *dihydroavicine*, m. p. 211—212·5° (Found: C, 72·5; H, 4·5; N, 4·2; NMe, 8·3%; *M* 382. $C_{20}H_{15}O_4N$ requires C, 72·1; H, 4·5; N, 4·2; NMe, 8·7%; *M* 333); $\lambda_{max.}$ in ethanol (log ε) 322 (4·33), 278 (4·50), 232 mμ (4·60). (Dihydroavicine gave a blue fluorescence in ultraviolet light in the solid or in solution). Elution with benzene–chloroform (3 : 1) gave a product (0·65 g.) which after two recrystallisations from concentrated ethanol solution, separated as

prisms of *oxyavicine*, m. p. 257—259°, solidifying to needles, m. p. 275—277° (the needle form was also obtainable by crystallisation from a less concentrated solution) (Found: C, 69·4; H, 3·8; N, 4·0; NMe, 7·0. $C_{20}H_{13}O_5N$ requires C, 69·2; H, 3·8; N, 4·0; NMe, 8·3%); $\lambda_{max.}$ in ethanol (log ε) 332 (4·19), 322 (4·21), 289 (4·76), 278 (4·70), 248 mμ (4·50). (Oxyavicine gave a purple fluorescence in ultraviolet light in the solid or in solution.)

Dihydroavicine from Oxyavicine.—To oxyavicine (0·1 g.), dissolved in sodium-dried tetrahydrofuran (15 ml.), was added lithium aluminium hydride (0·07 g.). The mixture was boiled under reflux in argon for 3 hr. Dilute hydrochloric acid was then added, and the mixture, after dilution with water, gave a precipitate, which, after recrystallisation from ethanol, yielded elongated prisms (0·07 g.), m. p. 210—212° alone or in admixture with dihydroavicine.

Oxyavicine from Dihydroavicine (via *Avicine Acetate*).—Dihydroavicine (0·35 g.) was dissolved in hot 50% acetic acid (30 ml.). Mercuric acetate (1·7 g.) was added, and the mixture was heated on the steam-bath for 2 hr. The precipitate was removed, and hydrogen sulphide was passed into the mother liquor. The black precipitate was discarded and the filtrate concentrated; it deposited bright yellow needles of *avicine acetate* (0·22 g.) which on recrystallisation from ethanol had m. p. 160° (decomp.; vac.; gas-heated copper block) (Found: C, 62·2; H, 4·9; N, 3·1. $C_{22}H_{17}O_6N,2H_2O$ requires C, 61·8; H, 5·0; N, 3·3%). To a solution of avicine acetate (0·1 g.) in hot water (20 ml.), was added a hot aqueous solution (10 ml.) containing potassium ferricyanide (0·2 g.) and potassium hydroxide (0·1 g.). The precipitate (0·08 g.) was collected and recrystallised from ethanol. Crystals, m. p. 257—259° (gradually re-solidifying to needles, m. p. 275—277°) alone or in admixture with oxyavicine, were obtained.

Salts of Avicine and Dihydroavicine.—(a) *Avicine ψ-cyanide.* To a solution of avicine acetate (0·1 g.) in water aqueous potassium cyanide was added. The precipitate (0·08 g.) was recrystallised from ethanol, giving needles of the *ψ-cyanide*, m. p. >340° (Found: C, 70·3; H, 4·1; N, 8·3. $C_{21}H_{14}O_4N_2$ requires C, 70·4; H, 3·9; N, 7·8%). (b) *Dihydroavicine hydrochloride.* Dihydroavicine (0·1 g.) was dissolved in chloroform (5·0 ml.), and concentrated hydrochloric acid (1·0 ml.) added. Removal of the chloroform under argon left a product which, when washed with alcohol under argon, gave the *hydrochloride* (0·11 g.), m. p. 255—258° (vac.; gas-heated copper block) (Found: C, 64·0; H, 4·4; Cl, 9·0. $C_{20}H_{15}O_4N,HCl$ requires C, 64·9; H, 4·4; Cl, 9·6%).

6,7,2′,3′-Tetrahydroxy-10-methyl-1,2-benzophenanthridone.—Oxyavicine (0·44 g.) was dissolved in boiling sodium-dried benzene (100 ml.). Anhydrous aluminium chloride (5 g.) was added and the mixture boiled under reflux for 7 hr. Addition of dilute hydrochloric acid gave a brownish precipitate (0·4 g.) which was recrystallised from ethanol. *6,7,2′,3′-Tetrahydroxy-10-methyl-1,2-benzophenanthridone* separated as pale brown crystals, m. p. 340° (Found: C, 67·0; H, 4·4; N, 4·1. $C_{18}H_{13}O_5N$ requires C, 66·9; H, 4·1; N, 4·3%). It gave a dark greyish-green colour with ferric chloride solution; a negative reaction was obtained in the Labat test. (Attempts to remove methylene groups from oxyavicine or dihydroavicine with phloroglucinol and sulphuric acid failed.)

6,7,2′,3′-Tetramethoxy-10-methyl-1,2-benzophenanthridone.—The above product (0·1 g.), suspended in ether, was treated with diazomethane in ether for 16 hr. A product separated as fine needles (0·09 g.), which after recrystallisation from ethanol had m. p. 251—253°, alone or in admixture with authentic 6,7,2′,3′-tetramethoxy-10-methyl-1,2-benzophenanthridone obtained from oxynitidine [1] (Found: C, 69·5; H, 5·5; N, 3·8; OMe, 32·5%. Calc. for $C_{22}H_{21}O_5N$: C, 69·6; H, 5·6; N, 3·7; 4OMe, 32·7%); $\lambda_{max.}$ in ethanol (log ε) 326 (4·22), 321 (4·26), 286 (4·84), 277 (4·75), 267 (4·72). (These values agree with those found for a sample of the product from oxynitidine.)

The authors thank Professor J. E. Driver for interest, Mrs. T. K. Leung (Government Herbarium, Hong Kong) for identification of plant material, and the Research Grants Committee of the University of Hong Kong for financial assistance.

UNIVERSITY OF HONG KONG, HONG KONG. [*Received, May 15th*, 1959.]

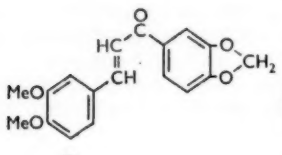
804. *An Examination of the Rutaceae of Hong Kong. Part IV.*[1a] *The Synthesis of Dihydronitidine.*

By H. R. Arthur and (Miss) Y. L. Ng.

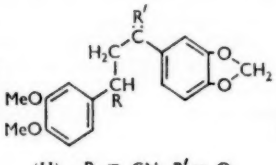
Dihydronitidine has been synthesised and the structures for nitidine and oxynitidine proposed in our earlier work have been confirmed.

We reported in Part II [1b] the occurrence of oxynitidine and a salt of nitidine in the bark of *Zanthoxylum nitidum* and the elucidation of the structures of these alkaloids by their conversion into a known compound. The structures have now been confirmed by synthesis of dihydronitidine using the route designed by Robinson and his co-workers [2] for compounds of the chelidonine–sanguinarine type, and used recently by Bailey and Worthing,[3] who synthesised chelerythrine.

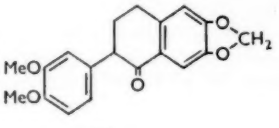
Acetopiperone (prepared as stated by Gopinath *et al.*[4]) and veratraldehyde on condensation gave the chalkone [2] (I), which was converted *via* the nitrile [2] (II) and the amide



(I)



(II) R = CN, R′ = O
(III) R = CO_2H, R′ = H_2



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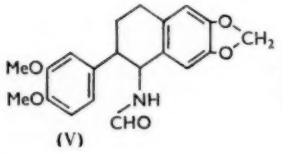

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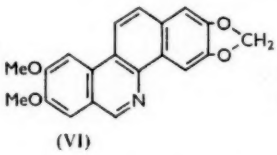

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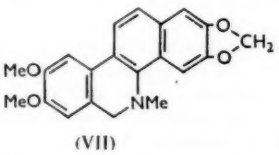

(VII)

into the corresponding keto-acid, which on reduction with hydrogen and palladium–charcoal in the presence of perchloric acid [3] gave the substituted n-butyric acid (III); cyclisation of this yielded a tetralone derivative (IV). Treatment with formamide and formic acid [2] afforded the substituted formamide (V) which on dehydration gave 3,4,11,12-tetrahydro-6,7-dimethoxy-4′,5′-methylenedioxy-1 : 2-benzophenanthridine; dehydrogenation to the benzophenanthridine (VI) was accomplished with 30% palladised charcoal.[5] The methosulphate of the base (VI), when reduced with zinc and hydrochloric acid, gave a product (VII) identical with dihydronitidine prepared from oxynitidine and nitidine acetate.[1b] Simple transformations by the methods [1b] used for dihydronitidine lead to syntheses of oxynitidine and nitidine acetate.

Experimental

Analyses were by Dr. Zimmermann, Melbourne. Unless otherwise stated, m. p.s were taken on a gas-heated copper block.

3,4-Dimethoxy-3′,4′-methylenedioxychalkone (I).—Acetopiperone (25 g.) and veratraldehyde (30 g.) were treated in ethanol (150 ml.) with 10% aqueous sodium hydroxide (30 ml.). The product, which slowly separated, was collected, and after crystallisation from ethanol was obtained as yellow needles (30 g.), m. p. 135°.

[1] (*a*) Part III, preceding paper; (*b*) Part II, *J.*, 1959, 1840.
[2] Richardson, Robinson, and Seijo, *J.*, 1937, 835.
[3] Bailey and Worthing, *J.*, 1956, 4535.
[4] Gopinath, Govindachari, Nagarajan, and Viswanathan, *J.*, 1957, 4760.
[5] Bailey, Robinson, and Staunton, *J.*, 1950, 227.

α-(3,4-*Dimethoxyphenyl*)-γ-(3,4-*methylenedioxyphenyl*)-γ-*oxobutyronitrile*.—To a solution of the chalkone (30 g.) in 2-ethoxyethanol (110 ml.) containing acetic acid (6·5 ml.) at 100° was added, during 3 min., potassium cyanide (12·5 g.) in water (45 ml.). Heating was continued for 10 min., then water (150 ml.) was added. The nitrile, which separated, was collected and after recrystallisation from ethanol was obtained as yellow needles (30 g.), m. p. 146°.

α-(3,4-*Dimethoxyphenyl*)-γ-(3,4-*methylenedioxyphenyl*)-γ-*oxobutyramide*.—A solution of the nitrile (30 g.) in acetic acid (200 ml.) was treated gradually with concentrated sulphuric acid (30 ml.). After dilution of the solution with water, the product separated; it was collected and crystallised from ethanol. The amide (25 g.) was obtained as needles, m. p. 177° (Found: C, 64·1; H, 5·4. Calc. for $C_{19}H_{19}O_6N$: C, 63·9; H, 5·4%).

α-(3,4-*Dimethoxyphenyl*)-γ-(3,4-*methylenedioxyphenyl*)-γ-*oxobutyric Acid*.—A solution of the amide (25 g.) in 7% aqueous sodium hydroxide (350 ml.) and ethanol (200 ml.) was boiled under reflux for 10 hr. and then acidified. The *keto-acid* (22 g.), which separated on cooling, was obtained as needles, m. p. 172° (from ethanol) (Found: C, 62·9; H, 5·0. $C_{19}H_{18}O_7$ requires C, 63·7; H, 5·0%).

2-(3,4-*Dimethoxyphenyl*)-1,2,3,4-*tetrahydro*-6,7-*methylenedioxy*-1-*oxonaphthalene*.—The keto-acid (11 g.) in acetic acid (110 ml.) containing 70% perchloric acid (2 ml.) was hydrogenated at 60°/1 atm. in the presence of 5% palladium–charcoal (2 g.) during 2 hr. The catalyst was removed and then most of the solvent under reduced pressure. Water was added to the residue, and the oily product was extracted with benzene. This extract, having been washed with water, was dried (Na_2SO_4) and then distilled on the steam-bath. The brown oil [α-(3,4-dimethoxyphenyl)-γ-(3,4-methylenedioxyphenyl)butyric acid] (8 g.) obtained, was boiled with phosphoryl chloride (20 ml.) for 4 min., and the mixture, having cooled, was poured on ice. The solid which separated was dissolved in chloroform and the solution was washed with aqueous sodium hydroxide, then with water, dried (Na_2SO_4), and evaporated. The residue, crystallised from ethanol, gave prisms (6·5 g.) of *the tetralone*, m. p. 165° (Found: C, 69·5; H, 5·6. $C_{19}H_{18}O_5$ requires C, 69·9; H, 5·6%).

2-(3,4-*Dimethoxyphenyl*)-1-*formamido*-1,2,3,4-*tetrahydro*-6,7-*methylenedioxynaphthalene*.—To a solution of the tetralone (6 g.) in formamide (15 ml.) and formic acid (0·8 ml.) was added ammonium sulphate (0·8 g.). The mixture was heated at 180° for 3 hr., formic acid (0·8 ml.) being added hourly. The cooled mixture was diluted with water, then extracted with chloroform. The washed extract was dried. Removal of its solvent gave an oil which was triturated with methanol (6 ml.). The colourless crystals which appeared overnight were collected and washed with acetone (10 ml.). The residue (3·5 g.) on recrystallisation from dioxan–ethanol (9 : 1) yielded the *formamide*, m. p. 178° (Found: C, 67·3; H, 5·9. $C_{20}H_{21}O_5N$ requires C, 67·6; H, 6·0%).

3,4,11,12-*Tetrahydro*-6,7-*dimethoxy*-2′,3′-*methylenedioxy*-1,2-*benzophenanthridine*.—The formamide (1·5 g.) was boiled with phosphoryl chloride (3 ml.) in toluene (10 ml.) for 15 min. The yellow solid which was deposited was washed with hot toluene and then suspended in hot methanol (15 ml.). Basification of the methanol suspension with ammonia gave white crystals (1 g.) which on crystallisation from methanol separated as colourless needles of the *product*, m. p. 188—189° (Found: C, 70·7; H, 5·3. $C_{20}H_{19}O_4N$ requires C, 71·2; H, 5·7%).

6,7-*Dimethoxy*-2′,3′-*methylenedioxy*-1,2-*benzophenanthridine*.—The tetrahydro-compound (0·9 g.) was heated with 30% palladium–charcoal (0·2 g.) at 240° for 30 min. The resulting solid was extracted with chloroform (4 × 30 ml.). The residue obtained on removal of the solvent from this extract, yielded, on crystallisation from pyridine, colourless needles (0·6 g.) of the *benzophenanthridine*, m. p. 273° (Found: C, 71·7; H, 4·5. $C_{20}H_{15}O_4N$ requires C, 72·1; H, 4·5%).

A solution of this product (0·5 g.) in xylene (5 ml.) and nitrobenzene (10 ml.) was boiled for a few minutes with methyl sulphate (1 ml.). A yellow precipitate was formed. Ether was added to the cooled suspension, then the solid was collected, washed with ether, and recrystallised from aqueous ethanol. The yellow *methosulphate*, m. p. 306—307° (decomp.), of 6,7-dimethoxy-2′,3′-methylenedioxy-1 : 2-benzophenanthridine (0·5 g.), was obtained as needles (Found: C, 57·8; H, 4·8. $C_{22}H_{21}O_8NS$ requires C, 57·5; H, 4·6%).

Dihydronitidine.—A solution of the methosulphate (0·4 g.) in water (60 ml.) and concentrated hydrochloric acid (4 ml.) was boiled under reflux with zinc powder (8 g.) in an atmosphere of argon for 5 hr., more hydrochloric acid (3 ml.) being added after each hr. The clear solution was then cooled to 0—5° and sealed under argon for 12 hr. The solid which separated

was collected, washed with water, and shaken with chloroform and ammonia. The chloroform extract was washed, dried, and evaporated in an atmosphere of argon. Crystallisation of the residue from ethanol gave prisms (0·2 g.) of *dihydronitidine*, m. p. 208—211° alone or in admixture with a sample prepared from a nitidine salt isolated from *Zanthoxylum nitidum* (Found: C, 72·0; H, 5·4. $C_{21}H_{19}O_4N$ requires C, 72·2; H, 5·5%). The light absorption for the synthetic compound in ethanol solution agreed with that earlier recorded.[1b]

The authors thank Professor J. E. Driver for interest, and the Research Grants Committee of the University of Hong Kong for financial assistance.

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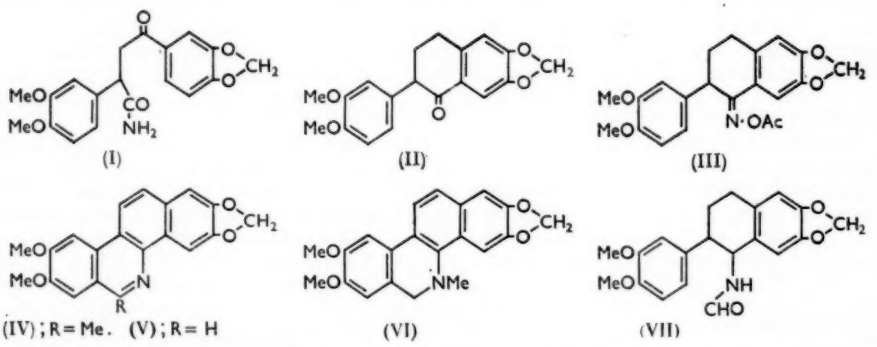
805. *Synthesis of Dihydronitidine.*

By K. W. GOPINATH, T. R. GOVINDACHARI, P. C. PARTHASARATHY, and N. VISWANATHAN.

Two syntheses of dihydronitidine are reported, starting from the tetralone (II).

IN a previous communication,[1] the single-step conversion of 2-aryl-1-tetralone oxime acetates into 9-methyl-1,2-benzophenanthridines was reported. During this study, it was found that the oxime acetate (III) gave a 40% yield of the 1,2-benzophenanthridine (IV). Meanwhile it was shown by Arthur, Hui, and Ng[2] that nitidine, a new alkaloid from *Zanthoxylum nitidum*, was 6,7-dimethoxy-10-methyl-2′,3′-methylenedioxy-1,2-benzophenanthridinium hydroxide, and we have confirmed this structure by two syntheses.

The tetralone (II) was prepared by the general method of Richardson, Robinson, and Seijo,[3] starting from acetopiperone and veratraldehyde. The amide[3] (I) was hydrolysed to the corresponding acid which was reduced by the Clemmensen method and then cyclised



to yield the tetralone (II). This was converted into the oxime, acetylated, and heated with acetic acid, acetic anhydride, and hydrogen chloride in a sealed tube, to yield the 9-methyl-1,2-benzophenanthridine (IV). In this connection, it is interesting that Schroeter[4] and Mills and Schofield[5] obtained the naphthylamines or their acyl derivatives from 1-tetralones and 1-phenyl-2-tetralones respectively. Our benzophenanthridine was formed by spontaneous cyclisation of the intermediate acetyl derivative and represents the first instance of a Morgan–Walls cyclisation proceeding without the use of conventional

[1] Gopinath, Govindachari, and Viswanathan, *Current Sci.* (*India*), 1959, **28**, 241.
[2] Arthur, Hui, and Ng, *Chem. and Ind.*, 1958, 1514.
[3] Richardson, Robinson, and Seijo, *J.*, 1937, 835.
[4] Schroeter, *Ber.*, 1930, **63**, 1308.
[5] Mills and Schofield, *J.*, 1956, 4213.

cyclisation reagents.[6] Oxidation of the compound (IV) with excess of selenium dioxide yielded the 9-carboxylic acid which was decarboxylated to give 6,7-dimethoxy-2',3'-methylenedioxy-1,2-benzophenanthridine (V). This was converted into the methosulphate and reduced with zinc and hydrochloric acid to yield 9,10-dihydro-6,7-dimethoxy-10-methyl-2',3'-methylenedioxy-1,2-benzophenanthridine (VI), identical (mixed m. p., ultraviolet and infrared spectra) with dihydronitidine.

The benzophenanthridine (V) was obtained in better overall yield from the tetralone (II) by the method of Bailey, Robinson, and Staunton.[7] By a Leuckart reaction, the tetralone yielded a separable mixture of 2-(3,4-dimethoxyphenyl)-3,4-dihydro-6,7-methylenedioxynaphthalene and the 1-formamido-derivative (VII). The former, on dehydrogenation, yielded 2-(3,4-dimethoxyphenyl)-6,7-methylenedioxynaphthalene, identified by its ultraviolet spectrum. The formamide was cyclised with phosphorus oxychloride in toluene to 3,4,11,12-tetrahydro-6,7-dimethoxy-2',3'-methylenedioxy-1,2-benzophenanthridine which was dehydrogenated to the benzophenanthridine (V) and converted into dihydronitidine by the same steps as in the earlier method.

Experimental

α-(3,4-Dimethoxyphenyl)-γ-(3,4-methylenedioxyphenyl)-γ-oxobutyronitrile.—A stirred solution of 3,4-dimethoxy-3',4'-methylenedioxychalkone[3] (10 g.) in 2-ethoxyethanol (65 ml.) containing acetic acid (2·5 ml.) was treated at 100°, during 3 min., with potassium cyanide (5 g.) in water (9 ml.). Heating was continued for a further 15 min. and water (100 ml.) was added, to give the nitrile (10 g.), m. p. 145—146°. (Richardson, Robinson, and Seijo[3] reported m. p. 144—146°. Their procedure offered difficulty for large-scale operations because of the sparing solubility of the chalkone in methanol and gave poorer yields of the nitrile.)

α-(3,4-Dimethoxyphenyl)-γ-(3,4-methylenedioxyphenyl)-γ-oxobutyric Acid.—The nitrile (5 g.) in acetic acid (35 ml.) was hydrolysed by concentrated sulphuric acid (5 ml.), in 15 min., to the amide[3] (5 g.), m. p. 178—180°. The amide (8 g.) was refluxed with alcohol (100 ml.) and 7% aqueous sodium hydroxide (100 ml.) for 8 hr. The solution was diluted with water (150 ml.) and extracted once with chloroform. The aqueous layer, on acidification, yielded the *acid* (7·5 g.), needles (from alcohol), m. p. 188—189° (Found: C, 64·0; H, 5·2. $C_{19}H_{18}O_7$ requires C, 63·7; H, 5·0%).

2-(3,4-Dimethoxyphenyl)-1,2,3,4-tetrahydro-6,7-methylenedioxy-1-oxonaphthalene (II).—The above keto-acid (10 g.), toluene (40 ml.), concentrated hydrochloric acid (53 ml.), zinc amalgam (24 g.), and 5% acetic acid (15 ml.) were refluxed for 48 hr., concentrated hydrochloric acid (10 ml.) being added every 10 hr. The toluene layer was separated, the aqueous layer was extracted once with benzene, and the combined toluene–benzene extracts were shaken with sodium carbonate solution. Acidification of the aqueous layer, followed by extraction with chloroform, gave α-(3,4-dimethoxyphenyl)-γ-(3,4-methylenedioxyphenyl)butyric acid (9 g.) as a pale yellow oil. This acid (2 g.) was heated with phosphorus oxychloride (5 ml.) at 100° for 15 min. and the red solution poured on ice. The product was extracted with chloroform, and the chloroform solution washed with sodium carbonate solution, then with water, dried (Na_2SO_4), and distilled. Chromatography of the residue in benzene over alumina gave the *tetralone* (0·8 g.), cubes (from dioxan–ethanol), m. p. 171—172° (Found: C, 70·1; H, 5·7. $C_{19}H_{18}O_5$ requires C, 69·9; H, 5·5%).

2-(3,4-Dimethoxyphenyl)-1,2,3,4-tetrahydro-1-hydroxyimino-6,7-methylenedioxynaphthalene.—The tetralone (1 g.), hydroxylamine hydrochloride (1 g.), and dry pyridine (5 ml.), heated at 100° for 5 hr. and poured into water, yielded the *oxime* (0·9 g.), needles [from benzene–light petroleum (b. p. 40—60°)], m. p. 170—171° (Found: C, 66·9; H, 5·6. $C_{19}H_{19}O_5N$ requires C, 66·9; H, 5·6%). The oxime (1 g.), heated at 100° for 3 hr. with acetic anhydride (2 ml.) and pyridine (2 ml.), yielded the *acetate* (0·9 g.), prismatic needles (from alcohol), m. p. 130—131° (Found: C, 65·8; H, 5·6. $C_{21}H_{21}O_6N$ requires C, 65·8; H, 5·5%).

6,7-Dimethoxy-9-methyl-2',3'-methylenedioxy-1,2-benzophenanthridine.—A solution of the oxime acetate (0·4 g.) in acetic acid (2 ml.) and acetic anhydride (3 ml.) was saturated with dry hydrogen chloride at 0° and heated at 95—100° in a sealed tube for 8 hr., then treated with water. The yellow solid obtained was filtered off, washed with aqueous alcohol, and basified

[6] Theobald and Schofield, *Chem. Rev.*, 1950, **46**, 175.
[7] Bailey, Robinson, and Staunton, *J.*, 1950, 2277.

with ammonia, to yield the *benzophenanthridine* (0·15 g.), needles (from pyridine), m. p. 233°, $\lambda_{max.}$ 230, 275, 350, 365 mμ (log ε 4·50, 4·94, 3·67, 3·36), $\lambda_{infl.}$ 305, 330 mμ (log ε 4·43, 4·03) (Found: C, 72·7; H, 5·1. $C_{21}H_{17}O_4N$ requires C, 72·6; H, 4·9%).

6,7-*Dimethoxy*-2′,3′-*methylenedioxy*-1,2-*benzophenanthridine*.—The methylphenanthridine (0·4 g.) in ethyl acetate (80 ml.) was refluxed with selenium dioxide (0·4 g.) for 6 hr. and the solvent removed. The residue was extracted with pyridine, and the solvent distilled off. The product was treated with 50% acetic acid, and the brownish solid obtained was filtered off and dried, to give crude 6,7-dimethoxy-2′,3′-methylenedioxy-1,2-benzophenanthridine-9-carboxylic acid (0·15 g.). This was heated with copper bronze (0·2 g.) at 250—260° for 10 min., then cooled. Sublimation at 250—260°/0·03 mm. gave the *benzophenanthridine* (0·06 g.), needles (from pyridine–ethanol), m. p. 277—278°, $\lambda_{max.}$ 230, 275, 315, 370 mμ (log ε 4.56, 4·80, 4·38, 3·40), $\lambda_{infl.}$ 330, 347 mμ (log ε 4·11, 3·73) (Found: C, 72·1; H, 4·5. $C_{20}H_{15}O_4N$ requires C, 72·1; H, 4·5%).

Dihydronitidine.—A solution of the above benzophenanthridine (75 mg.) in xylene (2 ml.) and nitrobenzene (3 ml.) was boiled for a short time, and methyl sulphate (0·2 ml.) was added to the boiling solution. A yellow precipitate was rapidly formed and after 3 min. the solution was cooled and ether (10 ml.) added. The solid was collected and washed with ether, to yield the methosulphate (75 mg.), m. p. 307° (decomp.). A mixture of the methosulphate (70 mg.), zinc (5 g.), concentrated hydrochloric acid (8 ml.), and water (100 ml.) was refluxed for 3 hr., concentrated hydrochloric acid (2 ml.) being added every hour. The mixture was cooled and extracted with ether. The ether layer was washed with water, dried (Na_2SO_4), and evaporated, to yield *dihydronitidine* (20 mg.), needles (from alcohol), m. p. 217—218°, undepressed by admixture with a sample of the natural product, $\lambda_{max.}$ 230, 280, 310 mμ (log ε 4·63, 4·59, 4·33) (Found: C, 71·8; H, 5·3. $C_{21}H_{19}O_4N$ requires C, 72·2; H, 5·4%).

2-(3,4-*Dimethoxyphenyl*)-1-*formamido*-1,2,3,4-*tetrahydro*-6,7-*methylenedioxynaphthalene*.—The tetralone (II) (2 g.) was heated under reflux at 180° for 3 hr. with formamide (5 ml.), formic acid (0·25 ml.), and ammonium sulphate (0·25 g.), formic acid (0·25 ml.) being added every 1 hr. The mixture was cooled, diluted with water, and extracted with chloroform. The dried (Na_2SO_4) chloroform extract gave, on removal of the solvent, a brownish gum which was chromatographed in benzene over alumina. The initial fractions of the eluate yielded, on evaporation, 2-(3,4-*dimethoxyphenyl*)-3,4-*dihydro*-6,7-*methylenedioxynaphthalene* (0·2 g.), needles (from methanol), m. p. 115—116°, $\lambda_{max.}$ 335 mμ (log ε 4·41) (Found: C, 73·5; H, 5·8. $C_{19}H_{18}O_4$ requires C, 73·5; H, 5·8%). Further elution of the column with benzene and finally with benzene containing 0·5% of ethanol yielded the *formamide* (0·9 g.), plates (from methanol), m. p. 187° (Found: C, 67·2; H, 5·6. $C_{20}H_{21}O_5N$ requires C, 67·6; H, 5·9%).

2-(3,4-*Dimethoxyphenyl*)-6,7-*methylenedioxynaphthalene*.—A mixture of the dihydronaphthalene (0·5 g.) and 30% palladised charcoal (0·2 g.) was heated at 240° for 30 min. in nitrogen. The mixture was cooled and extracted with chloroform, and the solvent removed. Crystallisation of the residue from ethanol gave 2-(3,4-*dimethoxyphenyl*)-6,7-*methylenedioxynaphthalene* (0·25 g.) as needles, m. p. 133°, $\lambda_{max.}$ 258, 297 mμ (log ε 4·65, 4·29) (Found: C, 74·3; H, 5·2. $C_{19}H_{16}O_4$ requires C, 74·0; H, 5·2%).

3,4,11,12-*Tetrahydro*-6,7-*dimethoxy*-2′,3′-*methylenedioxy*-1,2-*benzophenanthridine*.—The formamide (1 g.) in toluene (9 ml.) was refluxed gently for 30 min. with phosphorus oxychloride (3 ml.). The precipitated hydrochloride was filtered off, washed with ether, and basified with ammonia, to give the *tetrahydrobenzophenanthridine* (0·65 g.), needles (from pyridine–ethanol), m. p. 193—194°, $\lambda_{max.}$ 233, 287 mμ (log ε 4·67, 4·17) (Found: C, 71·3; H, 5·7. $C_{20}H_{19}O_4N$ requires C, 71·2; H, 5·6%).

6,7-*Dimethoxy*-2′,3′-*methylenedioxy*-1,2-*benzophenanthridine*.—The tetrahydrobenzophenanthridine (0·3 g.) was heated with 30% palladised charcoal (0·25 g.) at 230—240° for 30 min. in nitrogen. The product was repeatedly extracted with chloroform and the solvent evaporated. Crystallisation of the residue from pyridine–ethanol yielded the benzophenanthridine (0·15 g.), needles, m. p. and mixed m. p. with the previous specimen 277—278° (Found: C, 72·1; H, 4·5%).

We thank Dr. H. R. Arthur for a sample of dihydronitidine, the Government of India for a National Research Fellowship (to K. W. G.) and a Scholarship (to P. C. P.), and Mr. S. Selvavinayakam for microanalyses and infrared spectra.

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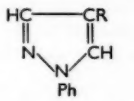
806. *Reactions of Some Pyrazole Derivatives.*

By I. L. Finar and K. Utting.

4-Formyl-1-phenylpyrazole has been converted into anils and these have been reduced to the corresponding amines. Some reactions of β-(1-phenyl-4-pyrazolyl)acrylic acid have also been investigated.

4-Formyl-1-phenylpyrazole [1] has been condensed with aniline [1] and the three isomeric monobromoanilines to yield the corresponding anils; [2] 2,4 3-tribromoaniline does not condense under the same conditions. The anils were reduced by sodium borohydride [3] to the corresponding amines, the toluene-*p*-sulphonyl derivatives of which were formed except by the *o*-bromo-amine. With malonic acid [4] the formylpyrazole gave the diacid (I) which in refluxing pyridine gave β-(1-phenyl-4-pyrazolyl)acrylic acid.[1] Bromination of this acid and its ethyl ester in acetic acid solution [5] gave the β-bromoacrylic acid (II) and the corresponding ester. Alkaline hydrolysis of the bromo-acid (II) gave β-oxo-β-(1-



(I) R = CH:C(CO$_2$H)$_2$
(II) R = CBr:CH·CO$_2$H
(III) R = CO·CH$_2$·CO$_2$H

phenyl-4-pyrazolyl)propionic acid (III) and 4-acetyl-1-phenylpyrazole, the latter also being obtained by decarboxylation of the former. β-(1-Phenyl-4-pyrazolyl)propionic acid has been obtained by Clemmensen reduction [6] of both the acrylic and the bromoacrylic acid. The acrylic acid reacted with hydroxylamine [7] to give a saturated β-amino-acid and underwent the Meerwein reaction [8] with diazonium salts to form the corresponding ethylenes.

Experimental

Anils of 4-Formyl-1-phenylpyrazole.—A mixture of the formylpyrazole (1·7 g., 0·001 mole) and *p*-bromoaniline (1·7 g. 0·001 mole) in absolute ethanol (20 c.c.) was warmed on a steam-bath for 15 min., then cooled, and the precipitate recrystallised from benzene or ligroin to give the p-*bromoanil* (2·9 g., 90%) as white needles, m. p. 168—169° (Found: C, 59·2; H, 3·7; N, 12·9; Br, 24·2. $C_{16}H_{12}N_3Br$ requires C, 58·9; H, 3·7; N, 12·9; Br, 24·5%). In the same way were obtained the m-*bromoanil* (90%) from methanol as plates, m. p. 125—126° (Found: C, 59·1; H, 3·7; N, 12·95; Br, 24·2%), and the o-*bromoanil* (80%) from methanol as needles, m. p. 101·5—102° (Found: C, 58·9; H, 3·9; N, 12·6; Br, 24·2%).

Reduction of the Anils.[3]—To a 5% (w/w) suspension of the *N*-(1-phenyl-4-pyrazolylmethylidene)aniline (1 mol.) in absolute methanol at 50° was added portionwise solid sodium borohydride (2 mol.); the vigorous reaction was allowed to subside between each addition of borohydride. When addition was complete the mixture was refluxed for 15 min., and then cooled, and an equal volume of water was added. The precipitate was collected and recrystallised from ethanol. The anil (2·0 g., 0·008 mole) yielded the *amine* (1·8 g., 90%) as plates, m. p. 70—71° (Found: C, 76·8; H, 6·1; N, 17·2. $C_{16}H_{15}N_3$ requires C, 77·1; H, 6·1; N, 16·9%). The amine yielded the *toluene*-p-*sulphonamide* as needles (from ethanol), m. p. 163—164° (Found: S, 7·75. $C_{23}H_{21}O_2N_3S$ requires S, 7·95%).

The p-*bromo-amine* (67%) was obtained as needles, m. p. 89—90° (Found: C, 58·4; H, 4·2; N, 13·0; Br, 24·1. $C_{16}H_{14}N_3Br$ requires C, 58·5; H, 4·3; N, 12·8; Br, 24·35%), yielding a *toluene*-p-*sulphonamide*, needles (from methanol), m. p. 162—162·5° (Found: S, 6·85.

[1] (*a*) Finar and Godfrey, *J.*, 1954, 2294; (*b*) Finar and Lord, *J.*, 1957, 3314.
[2] Lowy and Downey, *J. Amer. Chem. Soc.*, 1921, **43**, 346.
[3] Billman and Diesing, *J. Org. Chem.*, 1957, **22**, 1068.
[4] Knoevenagel, *Ber.*, 1898, **31**, 2598; Doebner, *Ber.*, 1900, **33**, 2140.
[5] Cf. Sudborough and Thompson, *J.*, 1903, **83**, 666.
[6] Clemmensen, *Ber.*, 1914, **47**, 51.
[7] Posner, *Ber.*, 1905, **38**, 2320; Steiger, *Org. Synth.*, Coll. Vol. III, 1955, p. 91.
[8] Meerwein, *J. prakt. Chem.*, 1939, **152**, 237; Bergmann, *J. Org. Chem.*, 1944, **9**, 408.

$C_{23}H_{20}O_2N_3BrS$ requires S, 6·65%); the m-*bromo-amine* (73%) formed plates, m. p. 86·5—87·5° (Found: C, 58·8; H, 4·3; N, 13·1; Br, 24·1%), yielding a *toluene*-p-*sulphonamide*, needles (from ethanol), m. p. 156—156·5° (Found: S, 6·8%), and the o-*bromo-amine* (50%) formed needles, m. p. 65—65·5° (Found: C, 58·4; H, 4·4; N, 12·85; Br, 24·1%).

1-*Phenyl*-4-*pyrazolylmethylenemalonic Acid* (I).—A mixture of the formylpyrazole (3·4 g., 0·02 mole) and malonic acid (4·2 g., 0·04 mole) was dissolved in pyridine (16 c.c.), and piperidine (4 drops) was added; the whole was left at room temperature for 5 days. Excess of 3N-hydrochloric acid was then added, and the precipitate collected and recrystallised several times from aqueous ethanol and then methanol to give the *diacid* (3·5 g., 67%) as a creamy powder, m. p. 212·5—214° (decomp.) (Found: C, 60·75; H, 3·75; N, 10·8. $C_{13}H_{10}O_4N_2$ requires C, 60·5; H, 3·9; N, 10·85%).

Decarboxylation of 1-*Phenyl*-4-*pyrazolylmethylenemalonic Acid* (I).—The methylenemalonic acid (0·25 g.) was refluxed in pyridine (10 c.c.) for 1 hr. The solution was acidified with 3N-hydrochloric acid, and the precipitate collected and recrystallised twice from aqueous acetic acid to give the acrylic acid as needles, m. p. and mixed m. p. 187—188°.

Ethyl β-(1-*Phenyl*-4-*pyrazolyl*)*acrylate*.—A mixture of β-(1-phenyl-4-pyrazolyl)acrylic acid [1a] (15·0 g., 0·07 mole), thionyl chloride (24·8 g., 0·21 mole), and benzene (60 c.c.) was refluxed for 1·5 hr., the excess of thionyl chloride and benzene evaporated under reduced pressure, and absolute ethanol (50 c.c.) added. The mixture was refluxed for 1 hr. and then cooled. The precipitate was collected and recrystallised from ethanol, to give the *ethyl ester* (15·2 g., 89%) as needles, m. p. 113—113·5° (Found: C, 69·3; H, 5·8; N, 11·8. $C_{14}H_{14}O_2N_2$ requires C, 69·4; H, 5·8; N, 11·6%).

β-*Bromo*-β-(1-*phenyl*-4-*pyrazolyl*)*acrylic Acid* (II) *and its Ethyl Ester*.—To the acrylic acid (5·0 g., 0·023 mole) in glacial acetic acid (25 c.c.) on the steam-bath was added dropwise bromine (3·75 g., 0·046 mole) in acetic acid (10 c.c.). After 15 min. the mixture was cooled and diluted with water. The precipitate was collected and recrystallised from ethanol, to give the *bromo-acrylic acid* (4·6 g., 66%), as needles, m. p. 223·5—224·5° (Found: C, 49·1; H, 2·85; N, 9·35; Br, 27·05. $C_{12}H_9O_2N_2Br$ requires C, 49·2; H, 3·1; N, 9·6; Br, 27·25%). In a similar manner was obtained the *ethyl bromoacrylate* (66%), as needles, m. p. 118—118·5° (Found: C, 52·3; H, 3·9; N, 8·4; Br, 24·9. $C_{14}H_{13}O_2N_2Br$ requires C, 52·35; H, 4·1; N, 8·7; Br, 24·9%).

Hydrolysis of β-*Bromo*-β-(1-*phenyl*-4-*pyrazolyl*)*acrylic Acid* (II).—The bromo-acid (5·0 g., 0·017 mole) and 2N-sodium hydroxide (200 c.c.) were refluxed for 1 hr., and then cooled; sufficient water was added to dissolve the precipitate. The mixture was extracted with ether (5 × 100 c.c.), and the extracts were dried (Na_2SO_4) and evaporated to dryness. After recrystallising from ethanol the solid (1·0 g.) had m. p. 127·5—128·5°, and was identified by m. p. and mixed m. p. as 4-acetyl-1-phenylpyrazole.[1b] Acidification of the alkaline solution gave a cream-coloured precipitate which when recrystallised from ethanol yielded β-*oxo*-β-(1-*phenyl*-4-*pyrazolyl*)*propionic acid* (III) as needles (2 g.), m. p. 154—155° (decomp.) (Found: equiv., 229·7. $C_{12}H_{10}O_3N_2$ requires equiv., 230·2). Refluxing this compound with dilute hydrochloric acid gave carbon dioxide and 4-acetyl-1-phenylpyrazole.

Reduction of (1-*Phenyl*-4-*pyrazolyl*)*acrylic Acid*.—Freshly prepared amalgamated zinc (20 g.) and the acrylic acid (5·0 g., 0·023 mole) were refluxed for 2·5 hr. with 5N-hydrochloric acid (30 c.c.), more acid (25 c.c.) being added during this period. After cooling, the solution was extracted with ether (5 × 50 c.c.). The ethereal solution was dried (Na_2SO_4) and evaporated, and the residual oil taken up in carbon tetrachloride from which β-(1-*phenyl*-4-*pyrazolyl*)-*propionic acid* crystallised as plates (3·5 g., 70%), m. p. 77—77·5° (Found: C, 66·4; H, 5·7; N, 12·8. $C_{12}H_{12}O_2N_2$ requires C, 66·65; H, 5·6; N, 13·0%).

β-*Amino*-β-(1-*phenyl*-4-*pyrazolyl*)*propionic Acid*.—Sodium (2·3 g., 0·1 g.-atom) was dissolved in absolute ethanol (80 c.c.), and hydroxylamine hydrochloride (6·95 g., 0·1 mole) in hot water (5 c.c.) was added followed by cooling. The precipitated sodium chloride was filtered off and washed with absolute ethanol (10 c.c.), and the main filtrate and washings were combined and added to β-1(-phenyl-4-pyrazolyl)acrylic acid (10·7 g., 0·05 mole). This mixture was refluxed for 9 hr.; dissolution was complete after 2·5 hr. and solid began to separate after 4 hr. The precipitate was collected and washed with ethanol (15 c.c.), ice-water (5 c.c.), and finally ethanol (15 c.c.), yielding the *amino-acid* (1·67 g., 14·5%), m. p. 234—235° (decomp.) (Found: C, 61·9; H, 5·65; N, 18·1. $C_{12}H_{13}O_2N_3$ requires C, 62·3; H, 5·6; N, 18·2%).

1-p-*Bromophenyl*-2-(1-*phenyl*-4-*pyrazolyl*)*ethylene*.—To *p*-bromoaniline (3·44 g., 0·02 mole) in concentrated hydrochloric acid (5 c.c.) and water (15 c.c.) at 3° was added sodium nitrite

(1·38 g., 0·02 mole) in water (4 c.c.) at 3°. This solution was added to a suspension of β-(1-phenyl-4-pyrazolyl)acrylic acid (4·3 g., 0·02 mole) and anhydrous sodium acetate (4·0 g., 0·02 mole) in acetone (100 c.c.), cooled to 8°, with stirring. Cupric chloride (0·9 g.) in water (3 c.c.) was then added and the mixture was stirred for 2 hr. at room temperature, then left for one day. The acetone and water were distilled off and the residual solid was extracted with dilute ammonia solution. The remaining solid was recrystallised from aqueous acetic acid and then benzene–light petroleum (b. p. 40—60°), to yield 1-p-*bromophenyl*-2-(1-*phenyl*-4-*pyrazolyl*)*ethylene* (3·5 g., 21%) as pale cream needles, m. p. 177—178° (Found: C, 63·1; H, 3·9; N, 8·5; Br, 24·3. $C_{17}H_{13}N_2Br$ requires C, 62·8; H, 4·0; N, 8·6; Br, 24·6%). In a similar manner was obtained 1-p-*methoxyphenyl*-2-(1-*phenyl*-4-*pyrazolyl*)*ethylene* (0·4 g., 7·2%) as plates (from ethanol), m. p. 150—151° (Found: C, 78·1; H, 6·0; N, 10·2. $C_{18}H_{16}ON_2$ requires C, 78·3; H, 5·8; N, 10·2%).

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807. *Aliphatic Friedel–Crafts Reactions. Part II.* The Acylation of Cyclopentene.*

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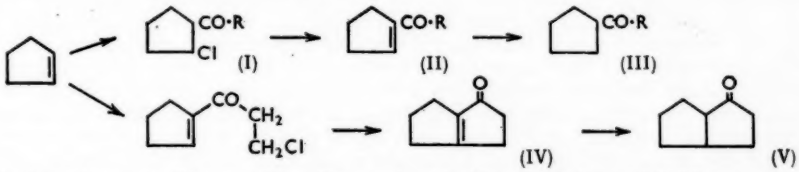
Cyclopentene is readily acylated with acid chloride–aluminium chloride complex in methylene chloride to provide an alkyl (or aryl) cyclopentenyl ketone in good yield. The product of interaction of 2-chloropropionyl chloride and cyclopentene affords bicyclo[3,3,0]oct-1(5)-en-2-one on cyclisation.

BY using Baddeley's modification [1] of Perrier's method [2] for the Friedel–Crafts reaction, a rapid homogeneous reaction is obtained, affording better yields than the more conventional technique in a solvent such as carbon disulphide. The acylation of ethylene and cyclohexene has been reported,[3,4] and this communication reports the acylation of cyclopentene with a variety of acid chlorides providing, after slow distillation from sodium carbonate,[5] the corresponding cyclopentenyl ketone (II). For comparison pent-1-ene has also been acetylated. The products have been quantitatively hydrogenated to the cyclopentyl ketones (III). Experimental procedure was simple and no precautions were taken against atmospheric moisture.



Cyclopentene readily reacts with acyl chloride–aluminium chloride complex in methylene chloride, the product containing some chlorine; improved yields are obtained at lower temperatures. Royals and Hendry [6] noted that in the acetylation of cyclohexene, the use of acetic anhydride is preferable to acetyl chloride in that subsequent dehydrohalogenation is easier; this seems to be the case in the acetylation of cyclopentene. Nightingale *et al.*[7] when preparing alkyl cyclohexenyl ketones observed persistent residual

* *J.*, 1958, 3922, should be regarded as Part I.

[1] Baddeley, *J.*, 1949, S 99.
[2] Perrier, *Bull. Soc. chim. France*, 1903, **31**, 859.
[3] Baddeley, Taylor, and Pickles, *J.*, 1953, 124.
[4] Taylor, *J.*, 1958, 3922.
[5] Christ and Fuson, *J. Amer. Chem. Soc.*, 1937, **59**, 893.
[6] Royals and Hendry, *J. Org. Chem.*, 1950, **15**, 1147.
[7] Nightingale, Milberger, and Tomisek, *ibid.*, 1948, **13**, 357.

chlorine after complete distillation of the products from sodium carbonate. Stevens and Farkas [8] isolated a little 4-chlorocyclohexyl methyl ketone when acetylating cyclohexene at low temperature in addition to the expected 1-chlorocyclohexyl methyl ketone; it is the former which is not readily dehydrochlorinated. The result can be explained by a carbonium ion mechanism.[9] A chlorine-free product will remain colourless, and the presence of chlorine is indicated by the product's slowly darkening.[7,10] Cyclopentenyl methyl ketone has been prepared previously, carbon disulphide being used as solvent.[10,11]

Treatment of the product of interaction of cyclopentene and β-chloropropionyl chloride with phosphoric acid in formic acid [12] gave bicyclo[3,3,0]oct-1(5)-en-2-one (IV), quantitatively hydrogenated to bicyclo[3,3,0]octan-2-one [13] (V). Cyclopentene and benzoyl chloride provide cyclopentenyl phenyl ketone,[14,15] which was reduced to cyclopentyl phenyl ketone; the unsaturated ketone has been cyclised [15] to 2,3-cyclopentanoindanone. The use of the ester chloride of a dibasic acid provides a route to acids of the type (III; R = $\cdot[CH_2]_n\cdot CO_2H$).

Interaction of pent-1-ene and cyclopentene with acylating agents at 0°, unless otherwise stated.

Acylating agent	Olefin	Product	Yield (%)
Me·COCl	Pent-1-ene	Me·CO·C_5H_9	43
$(Me\cdot CO)_2O$	,,	Me·CO·C_5H_9	46
Me·COCl	Cyclopentene [a]	Me·CO·C_5H_7	75(50 [d])
,,	,, [b]	Me·CO·C_5H_7	68
,,	,, [c]	Me·CO·C_5H_7	52
$(Me\cdot CO)_2O$	,,	Me·CO·C_5H_7	67
Et·COCl	,,	Et·CO·C_5H_7	50
$(Et\cdot CO)_2O$	,,	Et·CO·C_5H_7	55
Pr·COCl	,,	Pr·CO·C_5H_7	57
$Cl\cdot[CH_2]_2\cdot COCl$	,,	$Cl\cdot[CH_2]_2\cdot CO\cdot C_5H_7$	40
$MeO_2C\cdot[CH_2]_2\cdot COCl$	,,	$MeO_2C\cdot[CH_2]_2\cdot CO\cdot C_5H_7$	46
Ph·COCl	,,	Ph·CO·C_5H_7	62(53 [e])

[a] At −15°. [b] At 25°. [c] At 15°. [d] See ref. 10. [e] See ref. 15.

Experimental

Reaction of Acid Chlorides or Anhydrides with Olefins.—The acid chloride (0·2 mole) or acid anhydride (0·2 mole) was added to a suspension of finely powdered aluminium chloride (0·25 or 0·45 mole, respectively) in methylene chloride (150 ml.) with shaking. The resulting complex was decanted from excess of aluminium chloride, and poured through glass-wool into a cooled beaker. The olefin (0·2 mole) in methylene chloride (50 ml.) was then added dropwise, with stirring, at a convenient rate to maintain the required temperature. The mixture was kept for 5 min., and the product was then poured into dilute hydrochloric acid and ice. The organic layer was separated and dried (Na_2SO_4), the solvent removed, and the residue slowly distilled from anhydrous sodium carbonate (0·15 mole); occasionally a second distillation was necessary.

Acetyl chloride and pent-1-ene at 0° provided hept-3-en-2-one (9·5 g.), b. p. 50—51°/12 mm. [semicarbazone, m. p. 152° (Eccott and Linstead [16] record m. p. 152° for *cis*-form) (Found: N, 24·7. Calc. for $C_8H_{15}ON_3$: N, 24·9%)]. Acetic anhydride and pent-1-ene gave the same product (10·5 g.). A sample (1·74 g.) in ethanol (20 ml.) absorbed hydrogen (362 ml. corr. to S.T.P.; $C_7H_{12}O$ requires 349) in the presence of palladium (0·1 g.). The reduced product, heptan-2-one, gave a 2,4-dinitrophenylhydrazone, m. p. 89° (Johnson and Hager [17] record m. p. 89°).

[8] Stevens and Farkas, *J. Amer. Chem. Soc.*, 1953, **75**, 3306.
[9] Baddeley, *Quart. Rev.*, 1954, **8**, 355.
[10] Rapson and Robinson, *J.*, 1935, 1285.
[11] Rosenfielder and Grisberg, *J.*, 1954, 2955.
[12] Braude and Coles, *J.*, 1952, 1430.
[13] Linstead and Cook, *J.*, 1934, 946.
[14] Fuson, Johnson, and Cole, *J. Amer. Chem. Soc.*, 1938, **60**, 1594.
[15] Baker and Jones, *J.*, 1951, 787.
[16] Eccott and Linstead, *J.*, 1930, 914.
[17] Johnson and Hager, *Org. Synth., Coll. Vol. I*, 1st edn., p. 343.

Acetyl chloride and cyclopentene at −15° provided cyclopentenyl methyl ketone (16 g.), b. p. 168° [semicarbazone, m. p. 210°, and 2,4-dinitrophenylhydrazone, m. p. 203° (Heilbron *et al.*[18] record m. p. 212° and 203°, respectively)]. Acetic anhydride and cyclopentene at 0° gave the same product (14·5 g.). A sample (1·256 g.) absorbed hydrogen (261 ml., corr. to S.T.P.; $C_7H_{10}O$ requires 256 ml.) in the presence of palladium. The reduced product, cyclopentyl methyl ketone, gave a semicarbazone, m. p. 145° (Bartlett and Rosenwald [19] record m. p. 146—147°), and a 2,4-dinitrophenylhydrazone, m. p. 124° (Found: C, 53·5; H, 5·4; N, 19·0. Calc. for $C_{13}H_{16}O_4N_4$: C, 53·4; H, 5·5; N, 19·2%).

Propionyl chloride and cyclopentene at 0° provided cyclopentenyl ethyl ketone (13 g.), b. p. 60°/15 mm. [semicarbazone, m. p. 193° (Found: C, 59·6; H, 8·4; N, 23·0. Calc. for $C_9H_{15}ON_3$: C, 59·7; H, 8·3; N, 23·2%), and 2,4-dinitrophenylhydrazone, m. p. 210° (Found: C, 55·5; H, 5·3; N, 18·3. Calc. for $C_{14}H_{16}O_4N_4$: C, 55·3; H, 5·3; N, 18·4%)]. Propionic anhydride and cyclopentene at 0° gave the same product (14 g.). A sample (1·174 g.) absorbed hydrogen (206 ml., corr. to S.T.P.; $C_8H_{12}O$ requires 211 ml.). The reduced product, cyclopentyl ethyl ketone, gave a semicarbazone, m. p. 132° (Bedos [20] records m. p. 134°).

Butyryl chloride and cyclopentene at 0° provided cyclopentenyl propyl ketone (15·5 g.), b. p. 182° [2,4-dinitrophenylhydrazone, m. p. 164° (Found: C, 56·8; H, 5·7; N, 17·4. Calc. for $C_{15}H_{18}O_4N_4$: C, 56·6; H, 5·7; N, 17·6%)]. A sample (1·53 g.) absorbed hydrogen (239 ml. corr. to S.T.P.; $C_9H_{14}O$ requires 248 ml.). The reduced product, cyclopentyl propyl ketone gave a semicarbazone, m. p. 122° (Nazarov and Burmistrova [21] record m. p. 123—124°).

2-Methoxycarbonylpropionyl chloride and cyclopentene gave cyclopentenyl 2-methoxycarbonylethyl ketone (16·5 g.), b. p. 135°/15 mm. [semicarbazone, m. p. 150° (Found: C, 55·4; H, 7·0; N, 17·4. Calc. for $C_{11}H_{17}O_3N_3$: C, 55·2; H, 7·1; N, 17·6%)]. A sample (1·67 g.) absorbed hydrogen (214 ml. corr. to S.T.P.; $C_{10}H_{14}O_3$ requires 205 ml.). Cyclopentyl 2-methoxycarbonylethyl ketone gave a semicarbazone, m. p. 122° (Found: C, 54·9; H, 7·8; N, 17·3. Calc. for $C_{11}H_{19}O_3N_3$: C, 54·8; H, 7·9; N, 17·4%).

Benzoyl chloride and cyclopentene provided cyclopentenyl phenyl ketone (21·3 g.), b. p. 140°/12 mm. [2,4-dinitrophenylhydrazone, m. p. 168° (Baker and Jones [15] record m. p. 162—163°) and oxime, m. p. 140° (Smith and Scribner [22] record m. p. 138—142°)]. A sample (1·87 g.) absorbed hydrogen (262 ml., corr. to S.T.P.; $C_{12}H_{12}O$ requires 243 ml.). Cyclopentyl phenyl ketone gave a 2,4-dinitrophenylhydrazone, m. p. 142—143° (Nightingale and Maienthal [23] record m. p. 144·5—145·5°).

2-Chloropropionyl chloride and cyclopentene provided a product (12 g.), b. p. 108—112°/12 mm., which contained chlorine. It (5 g.) was added to a solution of phosphoric acid (3 g.) in 98% formic acid (6 g.), and the mixture kept at 90° under nitrogen for 12 hr. The mixture was then poured into water (100 ml.), and the organic material extracted with ether (2 × 25 ml.). The extracts were dried (Na_2SO_4) and, after removal of the ether, distillation of the residue gave bicyclo[3,3,0]oct-1(5)-en-2-one (4 g.), b. p. 87°/12 mm. [2,4-dinitrophenylhydrazone, m. p. 221° (decomp.) (Found: C, 55·3; H, 4·9; N, 18·7. Calc. for $C_{14}H_{14}O_4N_4$: C, 55·6; H, 4·6; N, 18·6%)]. A sample (1·01 g.) absorbed hydrogen (176 ml. corr. to S.T.P.; Calc. for $C_8H_{10}O$: 185 ml.). The reduced product, bicyclo[3,3,0]octan-2-one, gave a 2,4-dinitrophenylhydrazone, m. p. 112° after repeated crystallisation from ethyl acetate (Found: C, 55·1; H, 5·25; N, 18·5. Calc. for $C_{14}H_{16}O_4N_4$: C, 55·3; H, 5·30; N, 18·4%), and a semicarbazone, m. p. 181° (Found: N, 22·8. Calc. for $C_9H_{15}ON_3$: N, 23·2%) (Linstead and Cook [13] record m. p.s 116° and 181°, respectively).

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Coventry Technical College, Coventry. [*Received, July 8th*, 1959.]

[18] Heilbron, Jones, Toogood, and Weedon, *J.*, 1949, 1827.
[19] Bartlett and Rosenwald, *J. Amer. Chem. Soc.*, 1934, **56**, 1990.
[20] Bedos, *Compt. rend.*, 1949, **228**, 1441.
[21] Nazarov and Burmistrova, *Bull. Acad. Sci. U.S.S.R.*, 1947, 51.
[22] Smith and Scribner, *J. Amer. Chem. Soc.*, 1956, **78**, 3412.
[23] Nightingale and Maienthal, *ibid.*, 1950, **72**, 4823.

808. *Alkyls and Aryls of Transition Metals. Part II.*[1] *Platinum*(II) *Derivatives.**

By J. Chatt and B. L. Shaw.

Series of organoplatinum derivatives of the types $[L_2PtRX]$ and $[L_2PtR_2]$ have been prepared, where L is a tertiary phosphine or arsine, and R an aliphatic, aromatic, ethynyl, or substituted ethynyl group. They are stable to moist air and dilute acids, and generally their stabilities increase in the order of R = C≡CH < alkyl < phenyl ~ *p*-substituted phenyl < C≡CPh < *o*-substituted phenyl. The longer-chain alkyl groups and benzyl form less stable complexes than methyl, as is usual in organometallic compounds. The only dialkyl derivatives, $[L_2PtR_2]$, obtained have a *cis*-configuration, whatever the configuration of the starting material. Aryl radicals form both *cis*- and *trans*-compounds, and the acetylides only *trans*-$[L_2Pt(C{\equiv}CR)_2]$. Cleavage of the organic radicals by dry hydrogen chloride occurs one at a time from the dialkyl- and diaryl-platinum derivatives.

Other reactions of these compounds are described, and also the preparation of the first recorded aryl derivatives of platinum(IV), *viz.*, $(PEt_3)_2PtPh_2Cl_2$ and $(PEt_3)_2PtPh_2I_2$.

The dipole moments of the organoplatinum complexes are determined and a few anomalies discussed in terms of π-bonding between the platinum atom and the aryl groups.

Trimethylplatinum iodide, $(Me_3PtI)_4$, was one of the first of the very few alkyl derivatives of the transition metals to be described, and it is also one of the most stable.[2,3] It is therefore surprising that no ethyl or phenyl derivative is known, and that attempts to isolate them have failed.[4,5] In Part I [1] we described the preparation and properties of a new series of very stable complex compounds derived from the unknown dimethylplatinum(II), Me_2Pt, and methylplatinum(II) halides, MePtX (X = halogen). These are of the types *cis*-$[(PR'_3)_2PtMe_2]$ and *cis*- and *trans*-$[(PR'_3)_2PtMeX]$ (R = organic radical). *trans*-$[(PR'_3)_2PtMe_2]$ was much less stable. In view of the unique stability of the platinum(IV) methyl derivative mentioned above, it was of interest to see whether other organic groups could be introduced in place of the methyl groups in this series of organoplatinum(II) complexes, and our investigation of this is now reported.

We successfully introduced a range of hydrocarbon radicals, R, by the general reactions (1) and (2):

$$L_2PtCl_2 + RMgX \longrightarrow [L_2PtRX] + MgCl_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$L_2PtCl_2 + 2RMgX \longrightarrow [L_2PtR_2] + 2MgXCl \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

In these equations, L is a tertiary phosphine or arsine; lithio- or sodio-derivatives of the hydrocarbon radical, R, might be used instead of the Grignard reagent. The reactions were performed in ether, ether–benzene, or other appropriate solvent, the product was hydrolysed with dilute hydrochloric acid, and the organometallic complex isolated from the organic layer. Triphenylmethylsodium, cyclohexylmagnesium bromide, and cyclopentadienylsodium failed to give stable organoplatinum complexes. All other radicals, R, which we tried, gave organoplatinum(II) complexes, which are colourless, stable in the

* A brief account of this work formed part of a paper read before the American Chemical Society at its April, 1958, Meeting in San Francisco.

[1] Part I, Chatt and Shaw, *J.*, 1959, 705.
[2] Pope and Peachy, *Proc. Chem. Soc.*, 1907, **23**, 86; *J.*, 1909, **95**, 571.
[3] Cotton, *Chem. Reviews*, 1955, **55**, 551.
[4] Foss, personal communication.
[5] Gilman and Lichtenwalter, *J. Amer. Chem. Soc.*, 1939, **61**, 957.

presence of air, moisture, and cold dilute acids, soluble to varying degrees in organic solvents, and non-electrolytes in nitrobenzene solution.

Since the courses of the above reactions depend to some extent on the nature of the radicals, R, *i.e.*, whether they be alkyl, aryl, or ethynyl, it is convenient to describe these three types of organoplatinum(II) complex separately.

Alkyl and Benzyl Derivatives, cis-[L_2PtAlk_2], trans-[$L_2Pt(Alk)X$], *and their Benzyl Analogues*.—Since the methylplatinum complexes have been extensively investigated,[1] complexes of the other alkyls were investigated only cursorily. As in the preparation of the corresponding methyl derivatives, the product of reaction (1) has a *trans*-configuration and that of reaction (2) a *cis*-configuration, whatever the configuration of the starting material. Nevertheless, it is best to prepare *cis*-[$L_2Pt(Alk)_2$] from *cis*-[L_2PtCl_2] and alkyllithium, prepared from the alkyl chloride. *trans*-[L_2PtCl_2] is much less reactive, and Grignard reagents tend to give mixtures which are difficult to separate. Complexes were prepared with L = PMe_3, PEt_3, and $AsEt_3$ and R = Me, Et, Pr^n, Bu^n, and benzyl. Trimethylphosphine was used in order to promote crystallisability of the higher alkylplatinum complexes. The lowest homologue, *cis*-[$(PMe_3)_2PtMe_2$], is remarkably stable and volatile; it sublimes slowly in air at 110° and atmospheric pressure. The higher homologues and benzyl derivatives of types *cis*-[$(PR'_3)_2PtR_2$] and *trans*-[$(PR'_3)_2PtRCl$], are less stable than the corresponding methyl derivatives.

Cyclohexylmagnesium bromide reacts anomalously with *cis*-[$(PEt_3)_2PtCl_2$] in ether to form *trans*-[$(PEt_3)_2PtHBr$] [6] and presumably cyclohexene.

trans-[$(PPh_3)_2PtMeI$] was prepared by reaction of methyl iodide on [$(PPh_3)_3Pt$],[1] but the corresponding reaction with ethyl iodide gave only a poor yield of *trans*-[$(PPh_3)_2PtEtI$], and with benzyl iodide a complex mixture of products was obtained.

The benzyl complexes, *trans*-[$(PEt_3)_2Pt(CH_2Ph)Cl$] and *cis*-[$(PEt_3)_2Pt(CH_2Ph)_2$], differ from their methylplatinum analogues in some of their main reactions. They are more easily formed and more readily destroyed. Thus benzylmagnesium chloride undergoes reaction (2) under conditions where the purely aliphatic Grignard reagents undergo reaction (1), and both benzyl groups are more readily cleaved from the metal by reaction with magnesium iodide in ether [reaction (3)]. Benzyl iodide also cleaves both benzyl groups [reaction (4)]:

$$cis\text{-}[(PEt_3)_2Pt(CH_2Ph)_2] + 2MgI_2 \longrightarrow trans\text{-}[(PEt_3)_2PtI_2] + 2PhCH_2{\cdot}MgI \quad . \quad . \quad . \quad . \quad (3)$$

$$cis\text{-}[(PEt_3)_2Pt(CH_2Ph)_2] + 2PhCH_2I \longrightarrow trans\text{-}[(PEt_3)_2PtI_2] + 2PhCH_2{\cdot}CH_2Ph \quad . \quad . \quad . \quad (4)$$

The reaction analogous to (4) in the methylplatinum series gives a white mixture, probably of isomeric addition products, [$(PEt_3)_2PtMe_3I$], but certainly not containing any of the deep yellow di-iodide, *trans*-[$(PEt_3)_2PtI_2$].

In the methyl series, *cis*-[$(PEt_3)_2PtMeCl$] is readily obtained by the reaction of *cis*-[$(PEt_3)_2PtMe_2$] with dry hydrogen chloride in ether. The corresponding reaction in the benzyl series gives a mixture consisting mainly of *trans*-[$(PEt_3)_2Pt(CH_2Ph)Cl$], but containing some *cis*-isomer as indicated by the apparent dipole moment of 4·35 D. However, only the pure *trans*-isomer could be isolated by chromatography.

trans-[$(AsEt_3)_2Pt(CH_2Ph)Cl$] is obtained from *cis*-[$(AsEt_3)_2PtCl_2$] under exactly the same conditions as when *cis*-[$(PEt_3)_2Pt(CH_2Ph)_2$] is formed from *cis*-[$(PEt_3)_2PtCl_2$]. This may be caused by the greater lability of arsine complexes; the *cis*-[$(AsEt_3)_2Pt(CH_2Ph)Cl$] initially formed might thus isomerise to the less reactive *trans*-isomer before the second chlorine atom can be replaced.

Aryl Derivatives, cis- *and* trans-[L_2PtAr_2], *and* cis- *and* trans-[L_2PtArX].—The complexes derived from phenyl and *p*-substituted phenyl groups appear to be similar in their properties and only the phenyl derivatives were investigated in any detail. *m*-Substituted phenyl derivatives were not investigated. *o*-Substituted phenyls gave especially stable

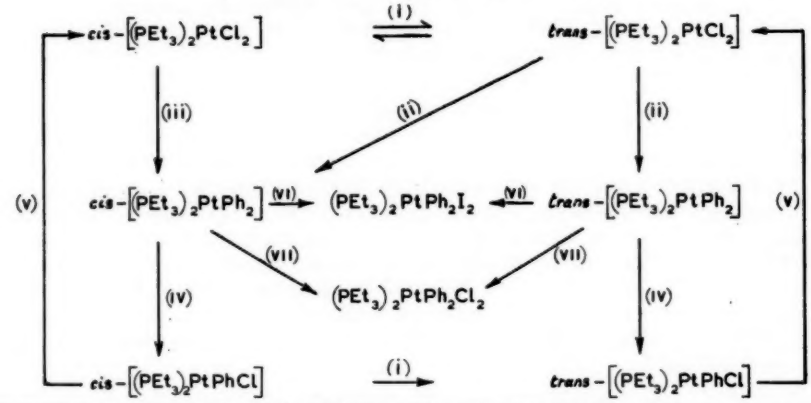
[6] Chatt, Duncanson, and Shaw, *Proc. Chem. Soc.*, 1957, 343; *Chem. and Ind.*, 1958, 859.

complexes and were therefore examined more closely than other substituted aromatic derivatives.

In general, the arylplatinum derivatives are more easily prepared and purified, and are more stable than the aliphatic compounds. We would expect the aryl groups to form bonds of partial double-bond character to a platinum(II) atom, and indeed the dipole moments on p. 4026 support the view that there is some double bonding. Such double bonding might account for the greater stability of the arylplatinum complexes and could be due to two causes: (*a*) increased M–C bond strength due to the addition of a certain amount of π-bonding between the metal and carbon atoms, and (*b*) increased splitting of the 5*d*-energy levels leading to stabilisation as discussed in Part I.

It is easier to obtain the diarylplatinum derivatives by reaction (2) than the monoaryl platinum derivatives by reaction (1). Reaction (2) occurs most readily with *cis*-$[L_2PtCl_2]$ (at 20°) to give a product of *cis*-configuration. With *trans*-$[L_2PtCl_2]$ the reaction is more sluggish, needing a higher temperature (80°), and the product is a mixture of *cis*- and

FIG. 1. *Preparation and reactions of phenylplatinum*(II) *derivatives.*



(i) Trace of PEt_3. (ii) PhLi at 20°, PhMgBr at 80°. (iii) PhLi, PhMgBr at 20°. (iv) Equiv. of HCl in ether. (v) Excess of HCl in ether. (vi) I_2. (VII) Cl_2.

trans-isomers. Aryl-lithiums react similarly but much more readily than Grignard reagents, and give better yields of the *cis*-isomers from both *cis*- and *trans*-$[L_2PtCl_2]$.

cis- and *trans*-$[L_2PtAr_2]$ are cleaved to the corresponding monoaryl complexes, $[L_2PtArCl]$, by dry hydrogen chloride in ether. This is the best method of preparing the *cis*-monoaryl derivatives, *e.g.*, *cis*-$[(PEt_3)_2PtPhCl]$, from which the *trans*-isomers are best prepared by isomerisation using a trace of the free phosphine.[7] The *trans*-diaryl complexes are not readily obtained in sufficient quantity to serve as raw materials for the preparation of the *trans*-monoaryl complexes.

Only the complexes having at least one anionic ligand such as $[(PR_3)_2PtCl_2]$ and $[(PR_3)_2PtRCl]$ are isomerised rapidly to the equilibrium mixture of *cis*- and *trans*-isomers by a trace of the free phosphine. The diaryls $[(PEt_3)_2PtPh_2]$ are not isomerised. This points to isomerisation through an ionic intermediate, *e.g.*, $[(PR_3)_3PtR]Cl$, rather than by the intramolecular rearrangement of a 5- or 6-co-ordinated intermediate, *e.g.*, $[(PR_3)_3PtRCl]$.

The reactions of the platinum(II) aryls exemplified by the phenyls are summarised in Fig. 1.

In contrast to *cis*-$(PEt_3)_2PtMe_2$, which loses a methyl group by reaction with one

[7] Cf. Chatt and Wilkins, *J.*, 1951, 2532.

molecule of iodine, both the *cis*- and the *trans*-$[(PEt_3)_2PtPh_2]$ add iodine to give the same stable Pt(IV) derivative $[(PEt_3)_2PtPh_2I_2]$. Chlorine behaves similarly. Thus are formed the first isolable arylplatinum(IV) derivatives. Their configuration, as determined from their dipole moments of 4·95 and 4·25 D, respectively, is shown in Fig. 2. The moments of the possible isomers of $[(PEt_3)_2Ph_2Cl_2]$, estimated as described for the corresponding methyl compounds in Part I, are: (*a*) 10·7, (*b*) 9·4, (*c*) 9·4, (*d*) 7·2, (*e*) 0·0, and (*f*) 3·7 D, where (*a*), (*b*), etc., are the configurations shown in Fig. 2 of Part I.[1] The phenylplatinic chloro-complex can only have the configuration (*f*) (*i.e.*, as in Fig. 2) because no other

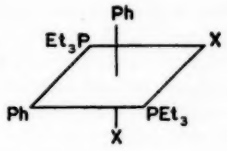


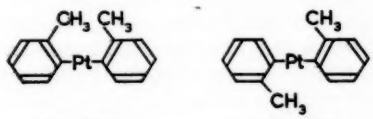
FIG. 2. *Configuration of the isomer* $[(PEt_3)_2PtPh_2X_2]$ (X = Cl, I), *obtained by the reaction of the halogen* X_2 *with either* cis- *or* trans-$[(PEt_3)_2PtPh_2]$

isomer has an estimated moment anywhere near the observed 4·25 D. The correspondence between this and the estimated moment of 3·7 D is reasonable, and the discrepancy is consistent with the expectation that dative π-bonding from the metal to the phenyl groups, which would render the latter more negative, is greater in the platinous than in the platinic series of complexes. The discrepancy might also be caused by different degrees of distortion from the ideally rectilinear arrangement of groups around the platinum atom, in the planar and octahedral complexes, and probably both effects contribute.

The complex iodides have rather higher moments than the corresponding chlorides, except where the halogen atoms are in *trans*-positions, and its moment of 4·95 D leaves little doubt that the $[(PEt_3)_2PtPh_2I_2]$ formed by the addition reaction has the same configuration as the chloride.

Methyl iodide reacts with both *cis*- and *trans*-$[(PEt_3)_2PtPh_2]$ to form a mixture of products.

ortho-*Substituted Phenyl Derivatives.*—The *o*-substituted phenylplatinum derivatives are especially stable, probably because the *ortho*-group hinders the attack of reagents at the platinum atom, and so the reactions of cleavage and decomposition are considerably slower than those of the phenyl and *para*-substituted phenyl complexes. *trans*-$[(PEt_3)_2Pt(o\text{-tolyl})_2]$ is also interesting stereochemically. Models show that there is not room for the *o*-tolyl groups to rotate about the Pt–C bonds, but that they are fixed by the bulky phosphine ligands so that the plane of the benzene rings is perpendicular to that containing the platinum atom and its four surrounding ligand atoms. Thus two isomers are possible as in Fig. 3, where the phosphine ligands, which would lie in front of and behind the plane of the paper, have been omitted for clarity. A model also shows that



syn-Form *anti*-Form

FIG. 3. syn- *and* anti-*forms of* trans-$[(PEt_3)_2Pt(o\text{-tolyl})_2]$ (*the* PEt_3 *groups have been omitted for clarity and lie above and below the plane of the paper*).

there is room for the methyl groups in the *syn*-form. Nevertheless, only one form was obtained, and this is probably the *anti*-form. The diple moment is not diagnostic in this case, because it is so small that the uncertainty in the atom polarisation introduces a significant error.

Attempts to prepare a dimesityl complex $[(PEt_3)_2Pt(mesityl)_2]$ failed, but the monomesityl complex, *cis*-$[(PEt_3)_2Pt(mesityl)Br]$, was easily obtained. A model shows that there is room for the two mesityl groups, and the fact that both *trans*-$[(PEt_3)_2Ni(mesityl)_2]$

and *trans*-$[(PEt_3)_2Co(mesityl)_2]$ are stable crystalline substances of planar configuration [8] is in agreement with this. The kinetic difficulty of introducing the second mesityl group was probably responsible for our not obtaining $[(PEt_3)_2Pt(mesityl)_2]$. A similar kinetic difficulty may be responsible for our failure to find two forms of *trans*-$[(PEt_3)_2Pt(o\text{-tolyl}_2]$, but in this case we have also been unable to obtain two forms of the palladium or nickel analogues.

Ethynyl Derivatives, trans-$[L_2Pt(C{\equiv}CR)_2]$.—These can be obtained by reaction (2) from the ethynylmagnesium halide in ether but they are most readily prepared by the reaction of the sodium acetylide ($RC{\equiv}CNa$) with $[L_2PtCl_2]$ in liquid ammonia.

They are stable, beautifully crystalline compounds, whose stabilities increase in the order R = H < Me < Ph. The substituted ethynyls have very strong bands in the infrared spectrum at *ca.* 2100 cm.$^{-1}$, and in $[(PEt_3)_2Pt(C{\equiv}CH)_2]$ at 1958 cm.$^{-1}$, indicating that these organic radicals have retained their triple bonds in the complex.

Styryl and Cyclopentadienyl Derivatives of Platinum(II).—Attempts to prepare styryl derivatives $[(PEt_3)_2Pt(CH{:}CHPh)Br]$ or $[(PEt_3)_2Pt(CH{:}CHPh)_2]$ by reactions (1) and (2) respectively led to the formation of *trans,trans*-1,4-diphenylbuta-1,3-diene, *trans*-$[(PEt_3)_2PtHBr]$, and *trans*-$[(PEt_3)_2PtBr_2]$, but no styrylplatinum compounds were found.

The reactions of cyclopentadienylsodium in tetrahydrofuran with *cis*-$[(PEt_3)_2PtCl_2]$ and with the bridged complex $[(PEt_3)_2Pt_2Cl_4]$ caused development of a dark red colour and precipitation of sodium chloride as though a coloured organoplatinum derivative had been formed, but attempts to isolate it led to general decomposition and blackening of the solution. This is surprising in view of the very wide occurrence of stable cyclopentadienyl-metal derivatives and the relatively high stability of complex alkyl and aryl derivatives of platinum(II).

The new organometallic complexes prepared during this investigation are listed in the Table, together with their melting points and electric dipole moments which were used to determine their configurations.

Electric Dipole Moments.—These, together with the moments of the methyl complexes recorded in Part I, show a number of interesting features, some of which must await further experiment for their explanation. Large dipole moments, measured in solution, may be appreciably in error owing to uncertainty in the effects of solvation or in the magnitude of atom polarisation, and to the assumptions made in deriving the equations by which they were calculated. Nevertheless, the differences between the moments of similar compounds appear to be reasonably accurate and here we are concerned only with differences.

Phenyl and Tolyl Complexes.—The organoplatinum groups lie at the negative end of the dipole as would be expected. This is shown by comparing the moments of the *cis*-ditolyl and *cis*-diphenyl complexes. Thus when the $^{+}C_{ar}{-}CH_3{}^{-}$ bond moment opposes the molecular moment expected from this asignment of polarity, as in *cis*-$[(PEt_3)_2Pt(p\text{-tolyl})_2]$, the molecular moment (6·75 D) is less than that of the analogous diphenyl complex (7·2 D), and when it reinforces the molecular moment as in *cis*-$[(PEt_3)_2Pt(o\text{-tolyl})_2]$, the molecular moment is greater (7·5 D). Quantitatively, if we assume that the Pt–C bonds are at an angle of 90° and that the moment [9] of toluene is 0·35 D, we can estimate the difference between the moments of *cis*-$[(PEt_3)_2PtPh_2]$ and its *p*-tolyl analogue to be $2 \times 0{\cdot}35 \cos 45° = 0{\cdot}49$ D as compared with the observed difference of 0·45 D. Also, on the assumption, in addition, that *cis*-*o*-tolyl groups do not rotate but are fixed in *anti*-configuration, an assumption not altogether justified, the difference between the moments of *cis*-$[(PEt_3)_2PtPh_2]$ and its *o*-tolyl analogue should be $2 \times 0{\cdot}35\cos 60°\cos 45° = 0{\cdot}25$ D (observed 0·3 D). These agreements are surprisingly satisfactory in view of the uncertainty in absolute values of the dipole moments involved in the calculations.

[8] Chatt and Shaw, *Chem. and Ind.*, 1959, 675.
[9] Wesson, "Tables of Electric Dipole Moments," The Technology Press, Massachusetts Institute of Technology, 1948, p. 36.

Chelate and "Free" Complexes.—The chelate complexes $[C_2H_4(PEt_2)_2PtPh_2]$ and $[C_2H_4(PEt_2)_2PtMe_2]$ have moments which are about 1·2 D greater than those of the corresponding complexes of monophosphines, *e.g.*, $[(PEt_3)_2PtPh_2]$. This difference is undoubtedly due to the rather smaller P–Pt–P bond angles which must occur in the chelate complex. The dipole moments of complexes containing the strongly dipolar P–Pt bonds must be very sensitive to slight changes in the angles between these bonds.

Phenyl and Methyl Complexes.—It might be expected that the difference between the moments of the Pt–CH_3 and Pt–Ph bonds would be about 0·35 D, the dipole moment of toluene. The observed differences are all greater than this, and the phenyl group appears to carry an appreciably greater negative charge, relative to the methyl group, than would be expected on the basis of their difference in electronegativity.

This is shown most markedly in the comparison of the moments of *cis*-$[(PEt_3)_2PtPh_2]$ (7·2 D) and $[C_2H_4(PEt_2)_2PtPh_2]$ (8·4 D) with those of their dimethylplatinum analogues (5·55 D and 6·7 D, respectively). The differences are about 1·7 D in each case instead of the 0·5 D which would be expected on the basis of the moment of toluene. The unexpectedly large difference between the moments of the corresponding *cis*-diaryl and *cis*-dialkyl complexes such as the phenyl and methyl discussed above might be due to the distortion of the P–Pt–P bond angle and would require the angle to be smaller in the diaryl than in the dialkyl complexes. It would then be a steric effect of the more bulky aryl groups. We do not consider this to be the sole reason for the large difference, even if it contributes to it, because the difference is the same whether we consider the "free" triethylphosphine complexes or the more strained chelate complexes. In our opinion it is more likely that dative π-bonding ($dp\pi$–$p\pi$) from the platinum to the aryl groups is sufficiently strong to account for the greater negative charge they appear to carry. In other words, there is a significant mesomeric drift of *d*-electrons from the platinum atom into the antibonding orbitals of the aromatic system. This explanation would also accord with the discrepancy, noted earlier in this paper, between the observed moments of the diphenyldichloroplatinic complex and that estimated from the observed moments of the pertinent platinous complexes.

When the moments of the complexes of the type $[L_2PtRX]$ are compared, it is again found that arylplatinum groups are rather more negatively charged than would be expected on the basis of the moments of the analogous methylplatinum complexes, but rather less so than would be expected on the basis of the moments of the above diarylplatinum complexes. Thus *trans*-$[(PEt_3)_2PtPhCl]$ and its bromo-analogue have moments which are about 0·8 D less than those of their methyl analogues, and cis-$[(PEt_3)_2PtPhCl]$ and its *o*- and *p*-tolyl analogues have moments 0·65, 0·75, and 0·55 D greater, roughly twice the expected values.

Halide Complexes.—It is apparent from the Table and from the moments of the methylplatinum complexes described in Part I that in an analogous series of halides, where the metal to halogen bonds contribute to the dipole moment, the moment increases along the series Cl < Br < I. This is the reverse of the normal sequence which is found in the gaseous hydrogen halides and in carbon–halogen compounds.[9]

This effect might be attributed to (*a*) increasing dative π-bonding from metal to halogen along the series Cl < Br < I, sufficiently strong to overcome and reverse the normal electrostatic effects of decreasing electronegativity, or to (*b*) increasing steric repulsion of the phosphine groups by the halogen atoms as they increase in size. This repulsion would tend to close the P–Pt–P bond angle slightly, so introducing a strong dipole moment from that atomic grouping. This moment would have its negative end pointing towards the halogen which caused it. Thus the larger halogen atom would appear to be the more negatively charged, provided that the increased polarity caused by the greater distortion of the P–Pt–P bond angle is sufficient to counteract and overcome the electrostatic effect of the lower electronegativity of the larger halogen atom.

At present there is conflicting evidence from infrared data as to whether the heavier

Melting points and dipole moments of complex organometallic compounds of platinum in benzene at 25°.

$10^5\omega$	$\Delta\varepsilon/\omega$	$10^3\Delta n/\omega$	$-\Delta v/\omega$	$_TP$	$_EP$	$_OP$	μ †
***cis*-[$(PMe_3)_2PtMe_2$], m. p. 130—131° (with sublimation)**							
9·122	9·34						
6·809	9·35						
			(0·47)	740 *	(65)	665 *	5·7 *
***cis*-[$(PMe_3)_2PtEt_2$], m. p. 89—91°**							
5·807	8·534						
8·641	8·543						
			(0·47)	780 *	(75)	693 *	5·8 *
***cis*-[$(PEt_3)_2PtEt_2$], m. p. 35—36°**							
8·463	6·890						
7·178	6·853						
			(0·47)	732 *	(103)	614 *	5·5 *
***trans*-[$(PEt_3)_2PtEtCl$], m. p. 53—55°**							
7·07	2·798						
4·91	2·795						
			(0·53)	399 *	(105)	278 *	3·7 *
***trans*-[$(PEt_3)_2PtEtI$], m. p. 75—77°**							
4·72	3·533						
7·48	3·519						
			(0·61)	484 *	(114)	353 *	4·15 *
***trans*-[$(PPh_3)_2PtEtI$], m. p. 257—262° (d.) §**							
4·653	2·839						
			(0·58)	615 *	(211)	372 *	4·25 *
***trans*-[$(PPh_3)_2PtEt(SCN)$], m. p. 235—243 (d.)**					(μ not measured)		
***cis*-[$(PMe_3)_2PtPr^n_2$], m. p. 95—97°**							
7·002	8·231						
5·157	8·166						
			(0·47)	757 *	(85)	659 *	5·7 *
***cis*-[$(PMe_3)_2PtBu^n_2$], m. p. 37—39°**							
4·829	7·68						
			(0·47)	761 *	(95)	652 *	5·65 *
***cis*-[$(PEt_3)_2Pt(CH_2Ph)_2$], m. p. 103—104°**							
5·406	8·374						
5·447	8·270						
5·183	8·200						
			(0·46)	1083 *	(143)	919 *	6·7 *
***trans*-[$(PEt_3)_2Pt(CH_2Ph)Cl$], m. p. 81—83°**							
5·498	1·984						
			(0·56)	306 *	(123)	164 *	2·8 *
***trans*-[$(AsEt_3)_2Pt(CH_2Ph)Cl$], m. p. 72—73·5°**							
4·59	1·768						
5·49	1·749						
			(0·56)	327 *	(143)	162 *	2·8 *
***cis*-[$(PEt_3)_2PtPh_2$], m. p. 151—154° (d.)**							
6·863	9·975						
7·962	10·05						
2·83	10·12						
18·53			0·464				
20·18			0·456				
29·89		6·88					
15·22		6·66		1229	139·7	1070	7·2
***trans*-[$(PEt_3)_2PtPh_2$], m. p. 176—180°**							
10·08	0·341						
8·288	0·305						
8·233	0·342						
25·73			0·433				
16·95			0·431				
56·22		6·41					
28·55		6·41		160·1	142·0	−3	~0

TABLE. (*Continued.*)

$10^3\omega$	$\Delta\varepsilon/\omega$	$10^3\Delta n/\omega$	$-\Delta v/\omega$	$_TP$	$_EP$	$_oP$	μ †
cis-[$(PEt_3)_2PtPhCl$], m. p. 133—136° (d.)							
2·279	16·57						
2·392	16·78						
			(0·56)	1804 *	(106)	1682 *	9·05 *
trans-[$(PEt_3)_2PtPhCl$], m. p. 105—107°							
5·020	1·532						
8·272	1·592						
5·285			0·568				
5·402			0·555				
22·34		3·66 ‡					
31·21		4·07 ‡		258·4	106	137·1	2·6
cis-[$(PPh_3)_2PtPh_2$], m. p. 144—160° (d.)							
3·581	6·55						
2·689	6·60						
			(0·43)	1270 *	(237)	997 *	7·0 *
cis-[$(AsEt_3)_2PtPh_2$], m. p. 110—111°							
11·48	8·29						
22·13		7·07					
29·48		7·63	(0·46)	1272 *	163 *	1084 *	7·25 *
trans-[$(AsEt_3)_2PtPh_2$], m. p. 138—141°							
8·69	0·331						
			(0·46)	180 *	(163)	−9 *	~0 *
trans-[$(AsEt_3)_2PtPhBr$], m. p. 91—94°							
5·317	1·723						
			(0·60)	330 *	(134)	176 *	2·9 *
trans-[$(AsPr^n_3)_2PtPh_2$], m. p. 130—133°							
6·366	0·273						
5·594	0·275						
			(0·46)	194 *	(163)	6 *	~0 *
cis-[$(Et_2P{\cdot}CH_2{\cdot}CH_2{\cdot}PEt_2)PtPh_2$], m. p. 210—215° (d.)							
5·013	14·075						
5·228	14·128						
5·642	14·077						
			(0·46)	1587 *	(129)	1439 *	8·4 *
cis-[$(PEt_3)_2Pt(o\text{-tolyl})_2$], m. p. 176—180° (d.)							
2·923	10·273						
2·633	10·251						
			(0·45)	1314 *	(147)	1145 *	7·5 *
trans-[$(PEt_3)_2Pt(o\text{-tolyl})_2$], m. p. 192—196°							
4·340	0·342						
10·81	0·319						
7·007			0·442				
4·847			0·448				
24·75		6·18 ‡					
15·09		5·61 ‡		165·8	146·7	0	~0
cis-[$(PEt_3)_2Pt(o\text{-tolyl})Cl$], m. p. 153—157°							
4·865	16·643						
4·754	16·693						
			(0·55)	1852 *	(111)	1724 *	9·15 *
cis-[$(PEt_3)_2Pt(p\text{-tolyl})_2$], m. p. 149—153° (d.)							
6·384	8·410						
6·861	8·385						
			(0·45)	1098 *	(147)	929 *	6·75 *
cis-[$(PEt_3)_2Pt(p\text{-tolyl})Cl$], m. p. 130—138 (d.)							
5·613	15·797						
5·660	15·765						
			(0·55)	1758 *	(111)	1630 *	8·95 *

TABLE. (*Continued.*)

$10^3\omega$	$\Delta\varepsilon/\omega$	$10^3\Delta n/\omega$	$-\Delta v/\omega$	$_TP$	$_EP$	$_OP$	μ †
cis-[$(PEt_3)_2Pt$(mesityl)Br], m. p. 182—185°							
5·435	14·90						
6·526	14·92						
			(0·60)	1872 *	(128)	1725 *	9·15 *
trans-[$(PEt_3)_2Pt(p$-chlorophenyl$)_2$], m. p. 228—230°							
7·031	0·461						
6·318	0·450						
			(0·52)	178 *	(149)	6 *	~0 *
trans-[$(PEt_3)_2Pt(C{\equiv}CH)_2$], m. p. 62—63°							
4·175	0·596						
			(0·47)	151 *	(121)	11 *	0·7 *
trans-[$(PEt_3)_2Pt(C{\equiv}CMe)_2$], m. p. 93—95·5°					(μ not measured)		
trans-[$(PEt_3)_2Pt(C{\equiv}CPh)_2$], m. p. 186—187° (d.)							
7·442	0·613						
7·374	0·677						
28·4		11·2					
26·8		10·4	(0·45)	209 *	169 *	15 *	0·9 *
trans-[$(AsEt_3)_2Pt(C{\equiv}CPh)_2$], m. p. 178—181° (d.)							
4·396	0·758						
			(0·45)	252 *	(190)	34 *	1·3 *
[$(PEt_3)_2PtPh_2Cl_2$], m. p. 153—155°							
5·840	3·467						
7·158	3·462						
4·500			0·456				
6·316			0·523				
17·85		9·46					
14·41		9·72		557	161	372	4·25
[$(PEt_3)_2PtPh_2I_2$], m. p. 149—152°							
8·978	3·676						
5·849	3·645						
5·927	3·705						
4·865			0·583				
13·81		11·8					
14·19		11·7		722	194	499	4·95

* Calculated by using estimated values of densities and refractivities. Estimated values are given in parentheses. Those of $-\Delta v/\omega$ are needed only approximately and were estimated from experience of measurements on similar compounds. Those of $_EP$ were estimated by using group refractivities (Vogel, *J.*, 1948, 1833, and references therein) and from our measured values for other similar compounds.

† For moments greater than *ca.* 4 D the margin of error is probably <0·1 D and is partly determined by the uncertainty in the atom polarisation, which may be up to 20% of the electron polarisation in complex compounds (the above values were calculated assuming it to be 15%). Similarly, the moments between 2·5 and 4 D will be in error by <0·2 D. The three complex acetylides appear to have small moments but, because the atom polarisation is difficult to estimate, the values of such moments are uncertain. It appears that either the atom polarisation is larger than usual in these compounds, or that a small amount of the *cis*- exists in equilibrium with the *trans*-isomer in solution.

‡ Molar refractivity for the yellow helium line (λ 5876·6 Å); the remainder are for the red helium line (λ 6678·1 Å).

§ (d.) = With decomposition.

halogens in platinous complexes carry a greater or lesser negative charge than chlorine,[10] and it is useless to speculate at this stage which of the above effects is mainly responsible for the anomalous sequence of increasing dipole moment with decreasing electronegativity of the halogen in complex organoplatinum halides.

[10] Chatt, Duncanson, Shaw, and Venanzi, *Discuss. Faraday Soc.*, 1958, **26**, 131.

Experimental

(Microanalyses are by Messrs. W. Brown and A. G. Olney, and Miss S. J. Lathwell, of these laboratories.)

The complexes $[(PR_3)_2PtCl_2]$ and $[(AsEt_3)_2PtCl_2]$ were prepared by reaction of the phosphine or arsine with K_2PtCl_4,[7,11] and are described in Gmelin's "Handbuch."[12] Spence Grade "H" alumina was used for chromatography. The m. p.s were determined on a Kofler hot-stage and are corrected. Reactions involving organo-lithium and -magnesium compounds were carried out in an atmosphere of nitrogen.

Preparation of Platinous Alkyls.—(1) *Platinous dialkyls: General method.* The finely divided platinous chloride complex, $[L_2PtCl_2]$ (*ca.* 2 g.; *cis*-isomer), suspended in dry benzene, was treated with an ether solution of the alkyl-lithium (10% excess; prepared from the alkyl chloride) at 20°. After 15 min., light petroleum (10 c.c.; b. p. 60—80°) was added, followed by water. The crude product isolated from the organic layer was purified by crystallisation. Prepared in this manner were: cis-*bis(trimethylphosphine)dimethylplatinum*, plates from light petroleum (b. p. 60—80°) (yield 62%) (Found: C, 25·65; H, 6·3. $C_8H_{24}P_2Pt$ requires C, 25·45; H, 6·4%); cis-*bis(trimethylphosphine)diethylplatinum*, prisms from light petroleum (b. p. 40—60°) (yield 41%) (Found: C, 29·95; H, 7·0. $C_{10}H_{28}P_2Pt$ requires C, 29·65; H, 6·95%); cis-*bis(triethylphosphine)diethylplatinum*, plates from methyl alcohol (yield 73%) (Found: C, 39·75; H, 8·25. $C_{16}H_{40}P_2Pt$ requires C, 39·25; H, 8·25%); cis-*bis(trimethylphosphine)di-n-propylplatinum*, prisms from light petroleum (b. p. 40—60°) (yield 75%) (Found: C, 33·3; H, 7·55. $C_{12}H_{32}P_2Pt$ requires C, 33·25; H, 7·45%); cis-*bis(trimethylphosphine)di-n-butylplatinum*, large prisms from light petroleum (b. p. 30—40°) on cooling the solution to −10° (yield 40%) (Found: C, 36·3; H, 8·0. $C_{14}H_{36}P_2Pt$ requires C, 36·45; H, 7·85%).

(2) trans-*Bis(triethylphosphine)chloro(ethyl)platinum*, *trans*-$[(PEt_3)_2PtEtCl]$. Ethylmagnesium chloride was prepared from magnesium (0·24 g.), ether (30 c.c.), a crystal of iodine, and ethyl chloride. A solution of *trans*-bis(triethylphosphine)dichloroplatinum (1·5 g.) in benzene (25 c.c.) was added and, after 45 minutes' stirring at 20°, the reaction mixture was cooled to −10° and hydrolysed with dilute hydrochloric acid. The organic layer was separated and dried ($MgSO_4$), and the crude product obtained on evaporation was chromatographed, elution with ether then giving trans-*bis(triethylphosphine)chloro(ethyl)platinum* (0·23 g.). After one crystallisation from aqueous methyl alcohol and two from light petroleum (b. p. 30—40°) it formed prisms (Found: C, 33·95; H, 7·15. $C_{14}H_{35}ClP_2Pt$ requires C, 33·9; H, 7·1%).

(3) trans-*Bis(triethylphosphine)iodo(ethyl)platinum*, *trans*-$[(PEt_3)_2PtEtI]$. Ethylmagnesium iodide was prepared from magnesium (0·48 g.), ether (15 c.c.), and ethyl iodide (3·5 g.). *cis*-Bis(triethylphosphine)dichloroplatinum (1·5 g.) was added and, after 1½ hours' stirring, hydrolysis with ice and hydrochloric acid gave trans-*bis(triethylphosphine)iodo(ethyl)platinum* (0·65 g.) as prisms from methyl alcohol (Found: C, 28·8; H, 6·1. $C_{14}H_{35}IP_2Pt$ requires C, 28·6; H, 6·0%).

(4) trans-*Bis(triphenylphosphine)iodo(ethyl)platinum*, *trans*-$[(PPh_3)_2PtEtI]$. Tris(triphenylphosphine)platinum (0·70 g., see Malatesta and Cariello[13]) was dissolved in ethyl iodide (10 c.c.). After 1 hr. the product was isolated by evaporation, digestion with methyl alcohol, and crystallisation from benzene, giving slightly impure trans-*bis(triphenylphosphine)iodo(ethyl)platinum* (0·31 g.) as needles (Found: C, 51·4; H, 3·85. $C_{38}H_{35}IP_2Pt$ requires C, 52·1; H, 4·05%). This iodide on treatment with potassium thiocyanate in acetone gave the corresponding *thiocyanate* as prisms (Found: C, 57·5; H, 4·35; N, 1·85. $C_{39}H_{35}NSP_2Pt$ requires C, 58·05; H, 4·35; N, 1·75%).

(5) cis-*Bis(triethylphosphine)dibenzylplatinum*, *cis*-$[(PEt_3)_2Pt(CH_2Ph)_2]$. Benzylmagnesium chloride was prepared from magnesium (0·96 g.), ether (20 c.c.), and benzyl chloride (5·56 g.). *cis*-Bis(triethylphosphine)dichloroplatinum (2·0 g.) and benzene (10 c.c.) were added and, after 1 hour's stirring, hydrolysis with hydrochloric acid and isolation gave cis-*bis(triethylphosphine)dibenzylplatinum* (1·27 g.) as plates from methyl alcohol (Found: C, 50·95; H, 7·35. $C_{26}H_{44}P_2Pt$ requires C, 50·9; H, 7·25%). Treatment of *trans*-bis(triethylphosphine)dichloroplatinum with benzylmagnesium chloride in benzene at 80° gave the same *cis*-dibenzylplatinum complex together with bibenzyl; even chromatography failed to disclose the presence of the *trans*-isomer.

(6) trans-*Bis(triethylphosphine)chloro(benzyl)platinum*, *trans*-$[(PEt_3)_2Pt(CH_2Ph)Cl]$. To a

[11] Jensen, *Z. anorg. Chem.*, 1936, **229**, 237.
[12] Gmelin's "Handbuch," Vol. 68, Part D, pp. 343—350 (1957).
[13] Malatesta and Cariello, *J.*, 1958, 2323.

solution of *cis*-bis(triethylphosphine)dibenzylplatinum (2·00 g.) in dry ether (20 c.c.) was added an ethereal solution of hydrogen chloride (22·0 c.c., 0·154N). Almost immediately a precipitate formed, which was collected and recrystallised from benzene–light petroleum (b. p. 60—80°) to give bis(triethylphosphine)chloro(benzyl)platinum (1·52 g., *cis*- and *trans*-mixture). This was chromatographed on alumina (100 g.) and elution with benzene then gave the pure trans-*isomer* as prisms (1·02 g.), m. p. 81—83°, from light petroleum (b. p. 40—60°) (Found: C, 41·1; H, 6·9. $C_{19}H_{37}ClP_2Pt$ requires C, 40·9; H, 6·7%).

(7) trans-*Bis(triethylarsine)chloro(benzyl)platinum*, *trans*-$[(AsEt_3)_2Pt(CH_2Ph)Cl]$. Benzylmagnesium chloride was prepared from magnesium (0·24 g.), ether (20 c.c.), and benzyl chloride (1·39 g.). Benzene (10 c.c.) and *cis*-bis(triethylarsine)dichloroplatinum (1·0 g.) were added and, after 1 hour's stirring at 20°, hydrolysis with dilute hydrochloric acid and isolation gave a crude product. The latter was chromatographed on alumina; elution with light petroleum (b. p. 40—60°) then gave bibenzyl and elution with ether gave trans-*bis(triethylarsine)chloro(benzyl)platinum* as cream plates (0·38 g.) from light petroleum (b. p. 60—80°) (Found: C, 35·45; H, 5·8. $C_{19}H_{37}ClAs_2Pt$ requires C, 35·35; H, 5·8%).

Fission of cis-*Bis(triethylphosphine)dibenzylplatinum by Magnesium Iodide.*—To a solution of magnesium iodide, prepared from iodine (0·60 g.), ether (15 c.c.), and excess of magnesium, was added *cis*-bis(triethylphosphine)dibenzylplatinum (0·20 g.); the mixture was then put aside for 1 hr. Hydrolysis with ice and hydrochloric acid and isolation gave *trans*-bis(triethylphosphine)di-iodoplatinum (0·18 g.) as yellow needles, m. p. 136—137°, from ethyl alcohol (Found: C, 20·7; H, 4·25. Calc. for $C_{12}H_{30}I_2P_2Pt$: C, 21·0; H, 4·4%).

Reaction between cis-*Bis(triethylphosphine)dibenzylplatinum and Benzyl Iodide.*—A mixture of benzyl iodide (0·34 g.) and *cis*-bis(triethylphosphine)dibenzylplatinum (0·55 g.) was heated at 100—120° for 15 min., cooled, and extracted with hot methyl alcohol. The extract was evaporated, and the residue distilled in a short-path still at 20 mm. (heating with a free flame). Bibenzyl, m. p. 49—52°, distilled first, followed by *trans*-bis(triethylphosphine)di-iodo-platinum; the latter formed yellow needles, m. p. 134—136°, from ethyl alcohol.

Reaction between Cyclohexylmagnesium Bromide and cis-*Bis(triethylphosphine)dibromoplatinum.*—Cyclohexylmagnesium bromide was prepared from magnesium (0·38 g.), cyclohexyl bromide (2·61 g.), and ether (30 c.c.). *cis*-Bis(triethylphosphine)dibromoplatinum (1·18 g.) was added and, after being stirred for 1 hr. at 20°, the mixture was hydrolysed with dilute hydrochloric acid. The residue obtained by evaporation of the organic layer, on crystallisation from methyl alcohol, gave *trans*-bis(triethylphosphine)bromohydroplatinum (0·23 g.), m. p. 89—91°, identical with an authentic sample.[6]

Preparation of cis-*Diarylplatinum Derivatives by using Arylmagnesium Bromides*; *General Method.*—The platinous chloride complex (*cis*-isomer) was added to a solution of the arylmagnesium bromide (100% excess) in ether–benzene. After being stirred for 1—1½ hr. at 20° the reaction mixture was cooled to 0° and hydrolysed with dilute hydrochloric acid. The organic layer was separated, dried ($MgSO_4$), and evaporated to dryness, and the residue purified by chromatography and/or crystallisation. Prepared in this manner were: cis-*bis(triethylphosphine)diphenylplatinum*, which was eluted from alumina by light petroleum (b. p. 40—60°) containing ether (5%) and formed needles from light petroleum (b. p. 80—100°) (yield 56%) (Found: C, 49·3; H, 6·85%; *M*, ebullioscopically in 1·5% benzene solution, 536; in 2·29% benzene solution, 570. $C_{24}H_{40}P_2Pt$ requires C, 49·2; H, 6·9%; *M*, 585); cis-*bis(triphenylphosphine)diphenylplatinum*, rhombs from benzene–light petroleum (b. p. 60—80°) (yield 61%) (Found: C, 66·3; H, 4·8. $C_{48}H_{40}P_2Pt$ requires C, 66·0; H, 4·6%).

trans-*Bis(triethylphosphine)diphenylplatinum.*—Phenylmagnesium bromide was prepared from magnesium (1·3 g.), bromobenzene (8·37 g.), and ether (40 c.c.); benzene (150 c.c.) was added, and most of the ether removed by distillation. After cooling, *trans*-bis(triethylphosphine)dichloroplatinum (3·5 g.) was added, and the mixture heated under reflux for 1 hr., cooled and, after hydrolysis with dilute hydrochloric acid, the crude product was isolated and chromatotraphed on alumina. Elution with light petroleum (b. p. 60—80°) afforded trans-*bis(triethylphosphine)diphenylplatinum*, which formed prisms (2·30 g.) from ethyl alcohol (Found: C, 49·3; H, 6·9%; *M*, ebullioscopically in 1·51% benzene solution, 538; in 2·54% solution, 566). Elution with ether gave *cis*-bis(triethylphosphine)diphenylplatinum which formed needles (0·23 g.) from methyl alcohol.

Action of Phenyl-lithium on trans-*Bis(triethylphosphine)dichloroplatinum.*—The *trans*-dichloride $[(PEt_3)_2PtCl_2]$ (3·4 g.), dissolved in benzene (30 c.c.), was treated under nitrogen with

an ethereal solution of phenyl-lithium (20 c.c., 0·756N). After 15 min. water was added, and the crude product isolated and chromatographed on alumina, as described above for the corresponding Grignard reaction. In this way *trans* (0·55 g.)- and *cis* (1·29 g.)-bis(triethylphosphine)-diphenylplatinum were isolated.

cis-*Bis(triethylphosphine)chloro(phenyl)platinum*, *cis*-[$(PEt_3)_2PtPhCl$].—*cis*-Bis(triethylphosphine)diphenylplatinum (1·11 g.) in benzene (15 c.c.) was treated with an ethereal solution of dry hydrogen chloride (5 c.c., 0·41N). After 15 min. the solution was evaporated to dryness, and the residue recrystallised from light petroleum (b. p. 80—100°) to give cis-*bis(triethylphosphine)chloro(phenyl)platinum* (0·76 g.) as glistening needles (Found: C, 39·95; H, 6·45. $C_{18}H_{35}ClP_2Pt$ requires C, 39·75; H, 6·5%). With an excess of dry hydrogen chloride under similar conditions *cis*-bis(triethylphosphine)diphenylplatinum gave an almost quantitative yield of *cis*-bis(triethylphosphine)dichloroplatinum.

trans-*Bis(triethylphosphine)chloro(phenyl)platinum*.—Dry hydrogen chloride was passed into a solution of *trans*-bis(triethylphosphine)diphenylplatinum (0·50 g.) in benzene (10 c.c.) for 1 min. The residue obtained on evaporation was recrystallised from light petroleum (b. p. 60—80°) to give trans-*bis(triethylphosphine)chloro(phenyl)platinum* as prisms (0·38 g.) (Found: C, 39·7; H, 6·5. $C_{18}H_{35}ClP_2Pt$ requires C, 39·75; H, 6·5%).

Isomerisation of cis- *to* trans-*Bis(triethylphosphine)chloro(phenyl)platinum*.—The *cis*-isomer (0·202 g.) was suspended in light petroleum (5 c.c., b. p. 60—80°) and triethylphosphine (0·05 c.c.) was added. After being heated to boiling, the solution was evaporated under reduced pressure, and the excess of triethylphosphine allowed to oxidise in air. Crystallisation of the residue from methyl alcohol afforded the *trans*-isomer as prisms (0·171 g.), m. p. 105—107°.

Addition Reactions.—(1) *Chlorine to* cis-*bis(triethylphosphine)diphenylplatinum*. The *cis*-platinum diphenyl complex (1·17 g.) in carbon tetrachloride was treated with a solution of chlorine in carbon tetrachloride (4 c.c., 0·50M). After 15 min. at 20° the solution was evaporated to dryness, and the residue recrystallised from light petroleum (b. p. 60—80°)–benzene, giving *bis(triethylphosphine)dichloro(diphenyl)platinum* (0·87 g.) as prisms (Found: C, 43·95; H, 6·15. $C_{24}H_{40}Cl_2P_2Pt$ requires C, 43·9; H, 6·15%).

(2) *Chlorine to* trans-*bis(triethylphosphine)diphenylplatinum*. The *trans*-platinum diphenyl complex on similar treatment with chlorine (1 mol.) in carbon tetrachloride gave the same bis-(triethylphosphine)dichloro(diphenyl)platinum as above (Found: C, 44·1; H, 6·2%).

(3) *Iodine to* cis-*bis(triethylphosphine)diphenylplatinum*. The latter (0·264 g.) in benzene (15 c.c.) was treated with a solution of iodine (0·113 g.) in benzene (10 c.c.). The colour of the iodine disappeared very rapidly. Evaporation and crystallisation of the residue from light petroleum (b. p. 80—100°) and then ethyl alcohol gave *bis(triethylphosphine)di-iodo(diphenyl)-platinum* (0·29 g.) as yellow prisms (Found: C, 34·4; H, 4·8%; *M*, ebullioscopically in 2% benzene solution, 816; in 3% benzene solution, 808. $C_{24}H_{40}I_2P_2Pt$ requires C, 34·35; H, 4·8%; *M*, 839). Treatment of *trans*-bis(triethylphosphine)diphenylplatinum with iodine under similar conditions gave an identical product to the above.

The Reaction between Phenylmagnesium Bromide and cis-*Bis(triethylarsine)dichloroplatinum*.—*cis*-Bis(triethylarsine)dichloroplatinum (1·18 g.) was added to a solution of phenylmagnesium bromide (0·015 mole) in ether (20 c.c.) and benzene (20 c.c.). After 1½ hours' stirring at 20°, hydrolysis with ice and hydrochloric acid and isolation gave a crude product, which was chromatographed on alumina (150 g.). Elution with light petroleum (b. p. 40—60°) gave trans-*bis(triethylarsine)diphenylplatinum* as needles (0·24 g.) from methyl alcohol (Found: C, 42·7; H, 6·0. $C_{24}H_{40}As_2Pt$ requires C, 42·8; H, 6·0%). Elution with light petroleum (b. p. 40—60°) containing ether (2%) afforded cis-*bis(triethylarsine)diphenylplatinum* as prisms (0·42 g.), from light petroleum (b. p. 60—80°) (Found: C, 42·8; H, 6·05%). Elution with ether gave trans-*bis(triethylarsine)bromo(phenyl)platinum* as prisms (0·16 g.) from methyl alcohol (Found: C, 31·85; H, 5·2. $C_{18}H_{35}BrAs_2Pt$ requires C, 31·95; H, 5·2%). Treatment of *trans*-bis(triethylarsine)dichloroplatinum (1·00 g.) under similar conditions to the above gave *trans*-(0·20 g.)- and *cis*(0·60 g.)-bis(triethylarsine)diphenylplatinum and *trans*-bis(triethylarsine)-bromo(phenyl)platinum (0·15 g.).

Bis(tri-n-propylarsine)diphenylplatinum [$(AsPr^n_3)_2PtPh_2$].—This was prepared from *trans*-bis-(tri-n-propylarsine)dichloroplatinum (1·18 g.) and phenylmagnesium bromide, and formed *prisms* (0·76 g.) from ethyl alcohol (Found: C, 47·3; H, 7·0. $C_{30}H_{52}As_2Pt$ requires C, 47·55; H, 6·9%).

Preparation of cis-*Diarylplatinum Derivatives by use of Aryl-lithiums*: *General Method*.—The

finely divided *cis*-platinous chloride complex, suspended in dry benzene, was treated with an ether solution of the aryl-lithium (10% excess) at 20°. After intermittent agitation for 15 min., benzene and water were added and the product was isolated from the organic phase and purified by chromatography and/or crystallisation. Prepared in this manner were: *cis*-bis(triethylphosphine)diphenylplatinum (yield 81%); cis-*bis(triethylphosphine)di*-o-*tolylplatinum*, needles from light petroleum (b. p. 80—100°) (yield 72%) (Found: C, 51·1; H, 7·35. $C_{26}H_{44}P_2Pt$ requires C, 50·9; H, 7·25%); cis-*bis(triethylphosphine)di*-p-*tolylplatinum*, prisms from methyl alcohol (yield 47%) (Found: C, 50·9; H, 7·35%); and 1,2-*bis(diethylphosphino)ethanediphenylplatinum*, needles from ethyl alcohol (yield 73%) (Found: C, 47·65; H, 6·35. $C_{22}H_{34}P_2Pt$ requires C, 47·55; H, 6·15%).

cis-*Bis(triethylphosphine)chloro*-(o-*tolyl*)*platinum*, *cis*-[$(PEt_3)_2Pt$(*o*-tolyl)Cl].—Treatment of *cis*-bis(triethylphosphine)di-*o*-tolylplatinum with hydrogen chloride (1·2 mol.) in ether–benzene for 1 hr. gave cis-*bis(triethylphosphine)chloro*-(o-*tolyl*)*platinum* as needles from benzene–light petroleum (b. p. 80—100°) (Found: C, 40·8; H, 6·75. $C_{19}H_{37}ClP_2Pt$ requires C, 40·9; H, 6·7%); yield 66%.

cis-*Bis(triethylphosphine)chloro*-(p-*tolyl*)*platinum*, *cis*-[$(PEt_3)_2Pt$(*p*-tolyl)Cl]. — Similarly, fission of *cis*-bis(triethylphosphine)-di-*p*-tolylplatinum with hydrogen chloride (1·05 mol.) in ether–benzene for ½ hr. afforded cis-*bis(triethylphosphine)chloro*-(p-*tolyl*)*platinum* as rhombs from benzene–light petroleum (b. p. 80—100°) (Found: C, 41·0; H, 6·75%); yield 67%.

cis-*Bis(triethylphosphine)bromo(mesityl)platinum*.—Mesitylmagnesium bromide was prepared from magnesium (0·77 g.), 2-bromomesitylene (6·38 g.), and tetrahydrofuran (30 c.c.). *cis*-Bis-(triethylphosphine)dichloroplatinum (4·0 g.) and benzene (20 c.c.) were added, and after being stirred for 1 hr. at 20° and heated under reflux for 15 min., the mixture was cooled and hydrolysed with dilute hydrochloric acid. Isolation then gave cis-*bis(triethylphosphine)bromo-(mesityl)platinum* (3·7 g.) as matted needles from benzene–light petroleum (b. p. 60—80°) (Found: C, 40·15; H, 6·65. $C_{21}H_{41}BrP_2Pt$ requires C, 40·05; H, 6·55%).

trans-*Bis(triethylphosphine)di*-p-*chlorophenylplatinum*.—This was prepared from *cis*-bis(triethylphosphine)dichloroplatinum and *p*-chlorophenylmagnesium bromide (4 mol.; reaction time 1 hr. at 20° +15 min. at 80°) and formed prisms from benzene (yield 46%) (Found: C, 44·35; H, 5·9. $C_{24}H_{35}Cl_2P_2Pt$ requires C, 44·05; H, 5·85%).

trans-*Bis(triethylphosphine)di(phenylethynyl)platinum*, *trans*-[$(PEt_3)_2Pt(C{\equiv}CPh)_2$]: *Grignard Method*.—Ethylmagnesium bromide was prepared from ethyl bromide (1·63 g.), magnesium (0·33 g.), and ether (30 c.c.). Phenylacetylene (1·39 g.) and benzene (25 c.c.) were added and the mixture was heated under reflux for 15 min., cooled to 20°, and *cis*-bis(triethylphosphine)dibromoplatinum (2·00 g.) added. After 17 hr. at 20° hydrolysis with ice and hydrochloric acid and isolation afforded trans-*bis(triethylphosphine)di(phenylethynyl)platinum* (1·67 g.) as needles, m. p. 186—187°, from light petroleum (b. p. 100—120°) (Found: C, 52·95; H, 6·35. $C_{28}H_{40}P_2Pt$ requires C, 53·05; H, 6·35%). The infrared spectrum (in a Nujol mull) had a strong band at 2100 $cm.^{-1}$ (C≡C stretching).

trans-*Bis(triethylphosphine)diethynylplatinum*, *trans*-[$(PEt_3)_2Pt(C{\equiv}CH)_2$].—A suspension of sodamide was prepared in a small Dewar vessel from sodium (0·46 g.) and liquid ammonia (100 c.c.). An excess of dry acetylene was passed in and then *cis*-bis(triethylphosphine)dichloroplatinum (1·0 g.) was added to the resultant solution of sodium acetylide. After 20 minutes' intermittent stirring, dry ammonium chloride (1·5 g.) was added, the mixture was poured into a beaker, and the ammonia allowed to evaporate. Isolation with ether then gave trans-*bis(triethylphosphine)diethynylplatinum* as needles (0·52 g.) from aqueous methyl alcohol (Found: C, 40·2; H, 6·85. $C_{16}H_{32}P_2Pt$ requires C, 39·9; H, 6·7%). The infrared spectrum in a Nujol mull included strong bands at 3275 (C≡C◄►H) and 1958 $cm.^{-1}$ (C≡C stretching). Similarly was prepared trans-*bis(triethylphosphine)dipropynylplatinum*, *trans*-[$(PEt_3)_2Pt(C{\equiv}CMe)_2$], as prisms (Found: C, 42·3; H, 7·1. $C_{18}H_{36}P_2Pt$ requires C, 42·4; H, 7·1%). The infrared spectrum (in Nujol mull) included a strong band at 2124 $cm.^{-1}$ (C≡C stretching). *trans*-Bis(triethylphosphine)di(phenylethynyl)platinum was also prepared in this way from *trans*-bis(triethylphosphine)di-iodoplatinum (88% yield) and from *cis*-bis(triethylphosphine)dichloroplatinum (79% yield).

trans-*Bis(triethylarsine)di(phenylethynyl)platinum*, *trans*-[$(AsEt_3)_2Pt(C{\equiv}CPh)_2$].—*trans*-Bis-(triethylarsine)dichloroplatinum (1·0 g.) in ether (25 c.c.) was added to a solution of sodium phenylacetylide, prepared from sodium (0·46 g.), ammonia (50 c.c.), and phenylacetylene (2·04 g.). The mixture was kept for 10 min., then ammonium chloride (1·5 g.) was added, and

the ammonia allowed to evaporate. Addition of water and benzene to the residue gave a pale, insoluble precipitate which in hot water decomposed to give ammonia, platinum, and phenylacetylene and may have been a salt-like acetylide similar to those prepared by Nast and his co-workers.[14] The benzene-soluble portion, after repeated recrystallisation from light petroleum (b. p. 80—100°) and ethyl alcohol, formed yellow needles (Found: C, 47·35; H, 5·8. $C_{28}H_{40}As_2Pt$ requires C, 46·6; H, 5·6%).

Reaction of β-Styrylmagnesium Bromide with cis-*Bis(triethylphosphine)dichloroplatinum.*—β-Styrylmagnesium bromide was prepared from magnesium (0·48 g.), β-bromostyrene (3·66 g.), a crystal of iodine, and ether (30 c.c.). Benzene (20 c.c.) and *cis*-bis(triethylphosphine)dichloroplatinum (2·0 g.) were added, and after being stirred for 1 hr. the mixture was hydrolysed with dilute hydrobromic acid, and the crude product isolated in the usual way and chromatographed on alumina. Elution with light petroleum (b. p. 40—60°) gave *trans,trans*-1,4-diphenylbuta-1,3-diene (0·28 g.) as plates, m. p. 150—155°, from methyl alcohol. Elution with light petroleum (b. p. 40—60°) containing ether (20%) gave *trans*-bis(triethylphosphine)bromohydroplatinum which formed prisms (0·24 g.), m. p. 95—97°, from light petroleum (b. p. 40—60°). Styrene and *trans*-bis(triethylphosphine)dibromoplatinum were also isolated from the chromatogram.

Determination of Dipole Moments.—These were determined as described in Part I [1] and are recorded in the Table. The margin of error is discussed in a footnote.

The authors thank Mr. T. Remmington and Miss I. Bates for assistance in measuring the dipole moments and Messrs. A. E. Field, C. J. Pembroke, and M. L. Searle for other experimental assistance.

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[14] Nast, Vester, and Griesshammer, *Chem. Ber.*, 1957, **90**, 2678.

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809. *A Magnetic Investigation of Cyanide Complexes of Nickel*(II) *in Solution.*

By M. S. Blackie and V. Gold.

Measurements of spin–lattice relaxation times of solvent protons by means of a wide-band nuclear magnetic resonance spectrometer have been used in a study of some cyanide complexes of nickel(II). The solution of nickel(II) cyanide in aqueous ammonia contains nickel entirely in the form of equimolecular amounts of $Ni(NH_3)_6^{2+}$ and $Ni(CN)_4^{2-}$ ions. Addition of potassium cyanide to this solution brings about a quantitative conversion of $Ni(NH_3)_6^{2+}$ into $Ni(CN)_4^{2-}$, the tetracyano-complex being the only nickel-containing species in solution when the stoicheiometric ratio CN/Ni is 4. Addition of cyanide beyond this point results in quantitative formation of $Ni(CN_6)^{4-}$, which is a catalyst for the relaxation of solvent protons about as effective as $Ni(NH_3)_6^{2+}$. When the stoicheiometric ratio CN/Ni is 6, all the nickel is in the form $Ni(CN)_6^{4-}$ and further cyanide addition up to a CN/Ni ratio of 7·33 is without effect.

Since magnetic-susceptibility measurements of aqueous solutions corresponding to the solute composition $K_4Ni(CN)_6$ have shown the presence of little, if any, paramagnetic solute, the observations indicate the occurrence of efficient spin–lattice relaxation involving a non-paramagnetic species.

The interconversion of diamagnetic and paramagnetic species in solution can be detected by the change in the apparent magnetic moment of the solute. This can be measured either by determining the bulk susceptibility of the ionic solution or by observing the spin–lattice relaxation time of the solvent protons by proton magnetic resonance spectroscopy.[1]

[1] Bloembergen, Purcell, and Pound, *Phys. Rev.*, 1948, **73**, 679.

The second technique is particularly suitable for the investigation of dilute solutions, since the phenomenon observed is a direct measure of the concentration and effective moment of the solute and not, as in bulk susceptibility measurements, a sum of solvent and solute susceptibilities. In the present work, nuclear magnetic resonance measurements of this kind have been applied to problems in the co-ordination chemistry of nickel(II), *viz.*, (i) the nature of the solution formed by dissolving nickel(II) cyanide in aqueous ammonia, and (ii) the species formed on addition of potassium cyanide to this solution and the equilibrium between them.

Experimental.—The construction and calibration of the nuclear magnetic resonance spectrometer and its adaptation for the measurement of proton relaxation times of aqueous solutions have been described.[2] The relaxation times were measured by either the "direct" or the "progressive saturation" method. Measurements by the former technique were restricted to relaxation times somewhat greater than 1 sec. The relaxation time was accurately related to the concentration of a relaxing species by the accepted equation [1] (see also ref. 2).

$$T_1^{-1} - T_0^{-1} = \alpha\mu_N^2 c \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where T_1 and T_0 are the relaxation times for the solution and the solvent respectively, and c is the concentration of the relaxing solute. For most measurements $T_1^{-1} \gg T_0^{-1}$. According to theory [1,3] μ_N is the effective magnetic moment of the paramagnetic relaxing solute, and α is a constant the value of which for water was obtained for our purposes by calibration of the apparatus with cupric ions for which μ_N was taken to have the value [4] 2·00 B.M. For the ammoniacal solutions the cuprammonium ion (as sulphate) with a reported [5] μ_N of 1·51 B.M. was used for all calibration. The values of α for the two media agree within experimental error.

TABLE 1. *Proton relaxation times for solutions of* $Ni(CN)_2,4H_2O$ *in aqueous ammonia* (*d* 0·880).

[Ni(II)] (M)	0	0·001	0·005	0·010	0·050	0·100
T_1 (obs.) (msec.)	5700	1600	400	215	44	21·5
$T_1^{-1} - T_0^{-1}$ (sec.$^{-1}$)	—	0·45	2·32	4·47	22·6	46·3

TABLE 2.

KCN added (mmoles)	CN/Ni	Vol. (V) of soln. (ml.)	$[Ni(NH_3)_6^{2+}]$ (calc.) (M)	$[Ni(CN)_6^{4-}]$ (calc.) (M)	10^3T_1 (sec.)	$T_1^{-1} - T_0^{-1}$ (sec.$^{-1}$)	$(T_1^{-1} - T_0^{-1})V/V_0$ (sec.$^{-1}$)
0	2·00	1·00	0·0500	—	21·5	46·3	46·3
0·050	2·50	1·50	0·0250	—	43	23·1	34·6
0·100	3·00	2·00	0·0125	—	85	11·6	23·2
0·125	3·25	2·25	0·0085	—	130	7·5	16·9
0·150	3·50	2·50	0·0053	—	215	4·5	11·2
0·175	3·75	2·75	0·0022	—	450	2·0	5·6
0·200	4·00	3·00	—	—	4800	0·03	0·1
0·233	4·33	4·00	—	0·0040	290	3·3	13·0
0·267	4·67	5·00	—	0·0066	195	5·0	24·8
0·300	5·00	6·00	—	0·0083	155	6·3	37·6
0·333	5·33	7·00	—	0·0095	140	7·0	48·3
0·367	5·67	8·00	—	0·0104	125	7·8	62·6
0·384	5·84	8·50	—	0·0108	120	8·2	69·3
0·400	6·00	9·00	—	0·0111	115	8·5	74·4
0·417	6·17	9·50	—	0·0105	125	7·8	74·4
0·433	6·33	10·00	—	0·0100	135	7·2	72·3
0·467	6·67	11·00	—	0·0091	145	6·7	73·9
0·533	7·33	13·00	—	0·0077	175	5·5	71·9

All measurements of proton relaxation times were performed with sample volumes of 0·23 cm.^{3} at room temperature (18—20°). Chemicals used were of "AnalaR" grade or otherwise of high purity. In all cases the level of paramagnetic impurities was insignificant.

The effect of added cyanide upon ammoniacal solutions of nickel(II) cyanide was studied

[2] Blackie, *Trans. Faraday Soc.*, in the press.
[3] Solomon, *Phys. Rev.*, 1955, **99**, 559.
[4] Conger and Selwood, *J. Chem. Phys.*, 1952, **20**, 383.
[5] Rivkind, *Doklady Akad. Nauk S.S.S.R.*, 1954, **98**, 97.

by making additions of different amounts of potassium cyanide solution from a micrometer syringe to 1 ml. portions of 0·1M-nickel solution. Table 2 indicates both the volumes used and the stoicheiometric concentrations achieved. Measurements on solutions were taken approximately ½ hr. after each addition of cyanide to ensure mixing and equilibration. Relaxation times were in fact constant and reproducible from about 15 min. after addition of cyanide. The results are given in Table 2.

Discussion

Table 2 shows that the relaxation time increases as cyanide ions are added to the ammoniacal solution of nickel(II) cyanide, up to the point where the concentration of cyanide groups in solution is four times that of nickel. On further addition of potassium cyanide the relaxation time decreases. This means that the first part of the cyanide addition removes relaxing ions until, when the ratio CN/Ni is 4, and the proton relaxation time is practically the same as for aqueous ammonia, the solution contains only diamagnetic species in significant amounts. The diamagnetism of all solutes at this stage is to be expected, since $Ni(CN)_4^{2-}$ is a diamagnetic ion and the reported value of its stability constant [6,7] requires that less than 0·1% of the nickel would be present in the form of the "free" (or aquated) nickel(II) ion. Our measurements thus confirm the low concentration of these ions (cf. ref. 8).

Since nickel(II) cyanide [$NiNi(CN)_4$] is insoluble in water but soluble in aqueous ammonia, it seemed probable that an ammoniacal solution of nickel cyanide would contain nickel in the form of the ions $Ni(NH_3)_6^{2+}$ and $Ni(CN)_4^{2-}$. The hexammine is paramagnetic and is therefore expected to be the relaxing species which disappears during the first stage of the cyanide addition. This conclusion is supported by a comparison of the relaxation times of ammoniacal solutions of nickel(II) cyanide and of hexamminenickel(II) sulphate. The relaxation time in a nickel(II) cyanide solution is found to be the same as that in a hexamminenickel(II) sulphate solution [2] of half the total nickel concentration (Fig. 1). This means that in the ammoniacal solution ammonia molecules do not displace any of the cyanide ligands of the tetracyanonickelate(II) ion.

By making the assumption that the reaction

$$Ni(NH_3)_6^{2+} + 4CN^- \longrightarrow Ni(CN)_4^{2-} + 6NH_3$$

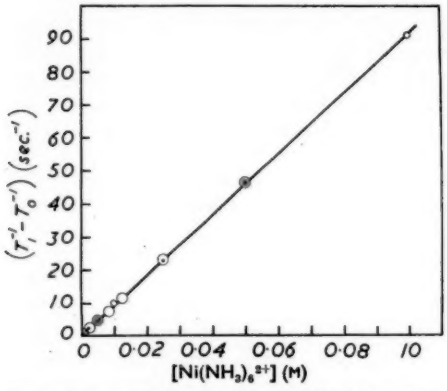
is stoicheiometrically complete at all stages of cyanide addition (and that no other complexes have to be considered during the destruction of the hexammine) it is possible to calculate the concentration of the paramagnetic hexamminenickel(II) ion at every stage. This very simple hypothesis is quantitatively confirmed by comparing the relaxation times of the solutions at the calculated concentrations with the measurements [2] on ammoniacal solutions of hexamminenickel(II) sulphate (Fig. 1).

The decrease in relaxation time which is found on addition of cyanide ions beyond the tetracyano-stage indicates the formation of another species capable of catalysing the proton-relaxation process. For the quantitative interpretation of these measurements it is necessary to allow for the fact that the addition of potassium cyanide solution not only raises the CN/Ni ratio in the solution but also causes a diminution of the overall nickel concentration by dilution. Since $(T_1^{-1} - T_0^{-1})$ is proportional to the concentration of relaxing ions [eqn. (1)], the dilution effect can be allowed for by multiplying all values of $(T_1^{-1} - T_0^{-1})$ by V/V_0 where V is the total volume of solution after cyanide addition and V_0 the initial volume of the nickel solution. In this way all measurements are related to the concentration of the initial solution of $[Ni(NH_3)_6]^{2+}[Ni(CN)_4]^{2-}$. The corrected values of $(T_1^{-1} - T_0^{-1})$ are given in the last column of Table 2 and related to the CN/Ni ratio in Fig. 2. The first, downward portion of the curve again illustrates the conversion of

[6] Latimer, "The Oxidation States of the Elements and their Potentials in Aqueous Solution," 2nd edn., Prentice-Hall, New York, 1952, p. 200.
[7] Hume and Kolthoff, *J. Amer. Chem. Soc.*, 1950, **72**, 4423.
[8] Masaki, *Z. phys. Chem.*, 1932, *A*, **159**, 223.

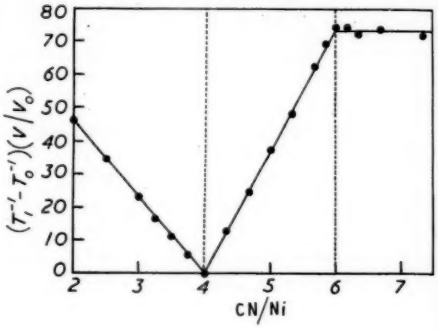
$Ni(NH_3)_6^{2+}$ into $Ni(CN)_4^{2-}$. This is seen to be complete when the ratio CN/Ni is **4**. The rectilinear course of the subsequent upward branch indicates that the new relaxing species is formed by a reaction which is also stoicheiometrically complete. The corrected relaxation time decreases until the ratio CN/Ni is **6** and thereafter the only effect of addition of cyanide is that of dilution. The species responsible for relaxation therefore contains six cyanide groups per nickel atom. Since a co-ordination number greater than **6** is improbable, the species will be referred to as $Ni(CN)_6^{4-}$. This conclusion is further confirmed

FIG. 1. *Proton relaxation by* $Ni(NH_3)_6^{2+}$.



Small circles: Measurements on $Ni(NH_3)_6^{2+}$ (ref. 2).
Large circles: Results of Table 2 (cols. 4 and 7).
Dots: Results of Table 1, $[Ni(NH_3)_6^{2+}]$ being taken as $\frac{1}{2}[Ni(CN)_2]$ stoich.

FIG. 2. *Proton relaxation in ammoniacal solutions of* $Ni(CN)_2$ + KCN.



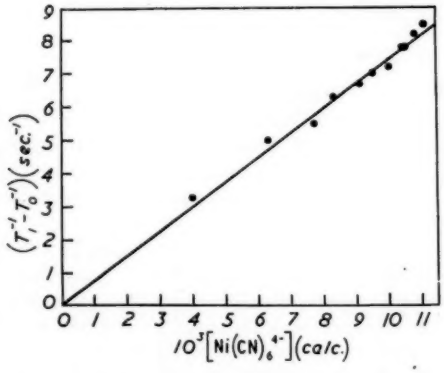


FIG. 3. *Proton relaxation by* $Ni(CN)_6^{4-}$ *(cols. 5 and 7, Table 2).*

by the rectilinear graph of $(T_1^{-1} - T_0^{-1})$ (after the minimum in Fig. 2) against the concentration of $Ni(CN)_6^{4-}$, calculated on the assumption that each addition of two moles of cyanide will generate quantitatively one mole of $Ni(CN)_6^{4-}$ (Fig. 3).

The agreement of all observations with the assumption that tetracyanonickelate(II) and hexacyanonickelate(II) are the only complexes formed between nickel and cyanide under our conditions rules out the occurrence of $Ni(CN)_5^{3-}$ in any significant concentration. The existence of this species has been suggested,[9] and evidence for its occurrence cited.[10]

[9] Martell and Calvin, "Chemistry of the Metal Chelate Compounds," Prentice-Hall, New York, 1952, p. 226.
[10] Morris and Nyholm, quoted by Nyholm, *Chem. Rev.*, 1953, **53**, 279.

Spectrophotometric results held to indicate the formation of $Ni(CN)_6^{4-}$ have recently been published.[11]

According to eqn. (1), the slope of the line in Fig. 3 is equal to $\alpha\mu_N^2$, whence it follows that the effective magnetic moment of $Ni(CN)_6^{4-}$ (for proton relaxation in ammoniacal solutions) has a value of 1·58 B.M. This result is to be compared with the value 1·75 B.M. observed for $Ni(NH_3)_6^{2+}$ under the same conditions.[2] Both these values are much lower than the " spin-only " moments, calculated on the assumption of two unpaired electrons. This kind of discrepancy has previously been noted in many cases.[4] It is generally accepted that hexamminenickel(II) has two unpaired electrons and one might thus conclude that the only slightly lower value now found for $Ni(CN)_6^{4-}$ indicates a similar electronic configuration and arrangement of ligands. However, approximate measurements of the susceptibility of aqueous solutions of $K_4Ni(CN)_6$ indicate that the magnetic dipole moment of this species must be very small or zero, and Professor Nyholm has personally informed us that this result has been confirmed in his laboratory. The two sets of measurements are not absolutely comparable since the susceptibility measurements relate to aqueous solutions whereas the relaxation studies concern ammoniacal solutions. Nevertheless, it does not seem likely that the nature of the hexacyano-complex is different in the two cases.

Whilst this observation does not in any way affect the validity of the conclusions concerning cyanide complexes of nickel(II) drawn from the relaxation measurements, it also raises a more important issue. The species $Ni(CN)_6^{4-}$ appears to be highly effective in inducing proton relaxation but seemingly does not do so by virtue of a permanent magnetic dipole moment. This indicates, more convincingly than the recognised discrepancies between magnetic moments deduced from susceptibility measurements and from relaxation measurements,[4] that the relaxation measurements provide some information about molecular structure which is additional to the information obtainable from susceptibility measurements. We are as yet unable to interpret this deduction.

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[11] Kišová and Čuprová, *Chem. Listy*, 1958, **52**, 1422; see also Cremoux and Mondain-Monval, *Bull. Soc. chim. France*, 1949, 700; cf. Adamson, *J. Amer. Chem. Soc.*, 1951, **73**, 5710.

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810. *The Stability of the* $Ni(CN)_6^{4-}$ *Ion.*

By M. S. BLACKIE and V. GOLD.

The equilibrium constants for the reactions

$$Ni(CN)_6^{4-} + Cd^{2+} \rightleftharpoons Ni(CN)_4^{2-} + Cd(CN)_2\downarrow$$
$$Ni(CN)_6^{4-} + 2Zn^{2+} \rightleftharpoons Ni(CN)_2\downarrow + 2Zn(CN)_2\downarrow$$

have been determined by measurements of proton relaxation times in the supernatant solutions. A combination of the results with Latimer's values of standard Gibbs free energies of formation of the species involved leads to somewhat discrepant values for the free energy of formation of $Ni(CN)_6^{4-}$. The discrepancy is thought to arise from inconsistencies in Latimer's tables, since the tabulated values are incompatible with the chemical identities of the precipitates formed on adding cadmium ions to hexacyanonickelate(II) solution.

NICKEL(II) ions in ammoniacal solutions are quantitatively converted into hexacyanonickelate(II) ions on addition of potassium cyanide so that the stoicheiometric ratio CN/Ni in solution is 6 or greater.[1] The reaction

$$Ni(CN)_4^{2-} + 2CN^- \longrightarrow Ni(CN)_6^{4-} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

[1] Blackie and Gold, preceding paper.

was found to be complete within the limits of detection by the nuclear magnetic resonance technique employed, so that it was impossible to estimate its equilibrium constant from the measurements. There was no evidence for the formation of $Ni(CN)_5^{3-}$ at any stage.

In the present work, information on the stability of the $Ni(CN)_6^{4-}$ ion has been obtained by adding to its solution metal ions with an affinity for cyanide comparable with that of nickel, in order to detach some of the cyanide groups from $Ni(CN)_6^{4-}$. Since the added metal ions, their cyanide complexes, and the nickel species formed in the reaction were all ineffective in catalysing proton relaxation, the proton relaxation times in the solutions were determined by the concentration of $Ni(CN)_6^{4-}$ which was therefore the only relaxing species present. In this way it was possible to deduce the concentration of $Ni(CN)_6^{4-}$ from proton relaxation times and hence to calculate equilibrium constants for the cyanide transfer reactions. The procedure is believed to be of wider applicability in inorganic co-ordination chemistry.

Experiments were carried out with four different diamagnetic (and non-relaxing) ions, *viz.*, Ag^+, Hg^{2+}, Zn^{2+}, and Cd^{2+}. With two of these (Ag^+ and Hg^{2+}) it was found that the addition of four equivalents per hexacyanonickelate(II) ion reduced the level of relaxing species below the limit of detection, so that the equilibrium constant could not be calculated. With zinc and cadmium ions, on the other hand, the reduced concentration of $Ni(CN)_6^{4-}$ ions could be determined and equilibrium constants were evaluated. The products of these reactions were identified by chemical tests. The measurements were performed on solutions of different ionic strengths and the conclusions are subject to the uncertainties arising from this cause.

Experimental.—The apparatus and general technique of measurement have been described in previous papers.[1,2]

Aqueous solutions of $K_4Ni(CN)_6$ were prepared by dissolution of $Ni(CN)_2$ in an aqueous solution containing the stoicheiometrically required amount of potassium cyanide. Measurements were carried out on the supernatant solutions obtained on mixing this solution with the requisite amounts of aqueous solutions of the sulphates of zinc, cadmium, silver, or mercury(II), and water. The stoicheiometric molar concentrations of nickel(II) and the added metal sulphate contained in the suspensions obtained on mixing are denoted by a and b, respectively. The concentration of the ion $Ni(CN)_6^{4-}$ remaining in solution, $(a - x)$, was deduced from the measured proton relaxation time on the assumption that no other species contribute to the relaxation. The results are summarised in Tables 1 and 2.

TABLE 1. *Proton relaxation times for the system* $Ni(CN)_6^{4-} + Cd^{2+}$.

$[Ni^{II}]_{total} = [Cd^{2+}]_{total}$ (a) (mole $l.^{-1}$)	T_1 (sec.)	$T_1^{-1} - T_0^{-1}$ (sec.$^{-1}$)	$[Ni(CN)_6^{4-}]$ * $(a - x)$	x	K_c'
0·25	0·041	24·1	0·0324	0·2176	207
0·50	0·027	36·7	0·0495	0·4505	184
1·00	$0·019_5$	51·0	0·0686	0·9314	198
				Mean	196

* $[Ni(CN)_6^{4-}] = \Delta T^{-1}/742$.

TABLE 2. *Proton relaxation times for the system* $Ni(CN)_6^{4-} + 2Zn^{2+}$.

$[Ni^{II}]_{total} = \frac{1}{2}[Zn^{2+}]_{total}$ (a) (mole $l.^{-1}$)	T_1 (sec.)	$T_1^{-1} - T_0^{-1}$ (sec.$^{-1}$)	$[Ni(CN)_6^{4-}]$ $(a - x)$	$10^{-3}K_s'$
0·010	0·71	1·12	0·00151	7·3
0·050	0·72	1·10	0·00148	7·7
0·100	0·72	1·10	0·00148	7·7
0·500	0·71	1·12	0·00151	7·3
				Mean 7·5

Discussion

The addition of two moles of zinc sulphate per mole of hexacyanonickelate(II) in solution produced a precipitate. The colourless supernatant solution proved to be

[2] Blackie, *Trans. Faraday Soc.*, in the press.

exceedingly dilute (in any solute) and it was therefore concluded that both zinc and nickel had been precipitated as cyanides according to the equation

$$\underset{a-x}{Ni(CN)_6^{4-}} + \underset{2(a-x)}{2Zn^{2+}} \longrightarrow \underset{x}{Ni(CN)_2}\downarrow + \underset{2x}{2Zn(CN)_2}\downarrow \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

This deduction is supported by the constancy of K'_z, defined as $K'_z = 1/[4(a-x)^3]$. Of the various possible reactions between Zn^{2+} and $Ni(CN)_6^{4-}$, (2) is the only one which has an equilibrium constant of this form.

The addition of one mole of cadmium sulphate per mole of hexacyanonickelate(II) in solution gave a white precipitate and a pale yellow supernatant solution. The precipitate was chemically identified as cadmium cyanide, free from nickel, and the supernatant solution contained nickel and a small amount of cadmium. The reaction is therefore

$$\underset{a-x}{Ni(CN)_6^{4-}} + \underset{a-x}{Cd^{2+}} \longrightarrow \underset{x}{Ni(CN)_4^{2-}} + \underset{x}{Cd(CN)_2}\downarrow \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

in agreement with the observed constancy of K_c', defined as $K_c' = x/(a-x)^2$. Of the various conceivable reactions between Cd^{2+} and $Ni(CN)_6^{4-}$ the only other reaction which has an equilibrium constant of this form is

$$Ni(CN)_6^{4-} + Cd^{2+} \longrightarrow Ni(CN)_2\downarrow + Cd(CN)_4^{2-} \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

and this alternative can be dismissed on the basis of the chemical tests. From the value of K_z', ΔG° for reaction (2) is $-10{\cdot}7$ kcal./mole. Similarly, K_c' leads to ΔG° for reaction (3) as $-3{\cdot}1$ kcal./mole.

It was hoped that a combination of K_z' and K_c' with the standard free energies of formation (ΔG°_f) of the other species involved in the reactions would lead to consistent values for ΔG°_f of $Ni(CN)_6^{4-}$, and hence to an approximate value for the stability constant of this ion. The following ΔG°_f values (relating to the usual standard states) are taken from Latimer's tables:[3] Zn^{2+}, $-35{\cdot}2$; $Zn(CN)_2$ (s), 29; $Zn(CN)_4^{2-}$, $100{\cdot}4$; Cd^{2+}, $-18{\cdot}6$; $Cd(CN)_2$ (s), $49{\cdot}7$; $Cd(CN)_4^{2-}$, 111; Ni^{2+}, $-11{\cdot}5$; $Ni(CN)_2$ (s), 37?; $Ni(CN_4)^{2-}$, $117{\cdot}1$ kcal./mole. From the zinc equilibrium, ΔG°_f for $Ni(CN)_6^{4-}$ is then given by $37(?) + 58 + 70{\cdot}4 + 10{\cdot}7 = 176{\cdot}1$ kcal./mole, a value which is subject to the reservation as to the value for $Ni(CN)_2$ (s), as indicated by a question mark in Latimer's book. The analogous calculation from the cadmium data is

$$\Delta G^\circ_f = 49{\cdot}7 + 117{\cdot}1 + 18{\cdot}6 + 3{\cdot}1 = 188{\cdot}5 \text{ kcal./mole}$$

The values obtained are unsatisfactory in two respects:

(i) The discrepancy of ~12 kcal. between the two results if exceedingly high, implying an uncertainty in the stability constant of $Ni(CN)_6^{4-}$ of about 10^{10}. The values for the equilibrium constant of the reaction

$$Ni(CN)_6^{4-} \rightleftharpoons Ni^{2+} + 6CN^-$$

are (from data for zinc) $10^{-37{\cdot}6}$ and (from data for cadmium) $10^{-27{\cdot}5}$. (A recent spectrophotometric determination[4] of this constant in the presence of 5M-potassium acetate or 10M-potassium nitrite gives a value of ~10^{-26}, but we are unable to follow the procedure by which this figure was obtained.)

(ii) Both of the values imply that the disproportionation reaction

$$2Ni(CN)_4^{2-} \longrightarrow Ni(CN)_2\downarrow + Ni(CN)_6^{4-}$$

should occur spontaneously in tetracyanonickelate(II) solutions of unit activity, and this conflicts with experience.

[3] Latimer, "The Oxidation States of the Elements and their Potentials in Aqueous Solution," 2nd edn., Prentice-Hall, Inc., New York, 1952.

[4] Kišová and Čuprová, *Chem. Listy*, 1958, **52**, 1422; *Coll. Czech. Chem. Comm.*, 1959, **24**, 862.

These contradictions led us to examine Latimer's values in relation to those of our observations which were entirely independent of the relaxation time measurements. This course seemed desirable in view of the novelty of the present application of the technique. So we used Latimer's free energies of formation to calculate the free energies of formation of all possible sets of products obtained from $(2Zn^{2+} + Ni^{2+} + 6CN^-)$ and from $(Cd^{2+} + Ni^{2+} + 6CN^-)$ to see whether the products with the supposedly lowest free energy of formation were in fact those observed in the two precipitation reactions. For the experiments with zinc the prediction from the free-energy values accords with experiment. For the cadmium experiments, the standard free energies of formation for three possible sets of products are:

$Ni(CN)_4^{2-} + Cd(CN)_2(s)$, 166·8 kcal./mole
$Ni(CN)_4^{2-} + \frac{1}{2}\,Cd^{2+} + \frac{1}{2}\,Cd(CN)_4^{2-}$, 154·0 kcal./mole.
$Ni(CN)_2(s) + Cd(CN)_4^{2-}$, 148(?) kcal./mole

The first line represents the products actually observed, but corresponds to the substance with the supposedly highest free energy of formation. The difficulty cannot simply be resolved by revision of the doubtful value for $Ni(CN)_2(s)$, which affects the third line only, but seems to indicate more far-reaching inconsistencies.

We thank Professor D. W. G. Style for his interest in this work.

King's College, Strand, London, W.C.2. [*Received, April 17th*, 1959.]

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811. *Purines, Pyrimidines, and Glyoxalines. Part XIV.* The Preparation and Some Reactions of α-Amino-α-cyanothioacetamide, leading to 6-Mercaptopurines and Adenines.*

By G. Shaw and (in part) D. N. Butler.

α-Amino-α-cyanothioacetamide has been prepared from α-cyanothioacetamide by reaction with nitrous acid followed by sodium dithionite in aqueous solution. The aminothioamide with cyanates or isothiocyanates gave linear ureas or thioureas, but with imidic esters gives glyoxalines, thiazoles, or more complex imidates. Further reactions lead to 6-mercaptopurines, adenines, and a thiazolopyrimidine, generally simply and in good yield.

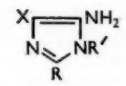
The previous paper in this series included a description of a one-step, general, unambiguous synthesis of 1-substituted 5-aminoglyoxaline-4-carboxyamides (Ia; R = H or Me) from linear imidates (II; R = H or Me) and primary amines including D-glycosylamines where the 1-substituent is derived from the amine. The ready and well-known conversion of aminoglyoxalinecarboxyamides into purines, makes the synthesis also one of 9-substituted 6-hydroxypurines of the hypoxanthine and xanthine type.

We have been interested in extending these reactions to include syntheses of similar intermediates which would lead eventually to 6-mercaptopurines and to adenines. Previous methods require relatively drastic treatment of intermediates with phosphoryl halides or phosphoric sulphide, and we sought methods which could be used under mild conditions, preferably in aqueous or alcoholic media. A much sought intermediate for the synthesis of adenines and other compounds through aminoglyoxalinenitriles has been aminomalononitrile, but many attempts to prepare this substance gave only dimeric products.[1] An alternative route would include desulphurisation of the corresponding

* Part XIII, *J.*, 1959, 1648.

[1] Cf. Cook and Smith, *J.*, 1949, 3001.

thioamide (III) which at the same time offers a route to the thiocarboxyamides (Ib). These would be expected to yield nitriles under mild conditions and to be a source of 6-mercaptopurines and adenines. We now record a convenient preparation of the thioamide (III) and some of its reactions.



(Ia) X = $CO\cdot NH_2$
(Ib) X = $CS\cdot NH_2$
(Ic) X = CN

$EtO\cdot CR{=}N\cdot CH(CN)\cdot CO\cdot NH_2$ (II)

$H_2N\cdot CH(CN)\cdot CS\cdot NH_2$ (III)

$HON{=}CH(CN)\cdot CS\cdot NH_2$ (IV)

α-Cyanothioacetamide [2] with nitrous acid gave the crystalline hydroxyimino-derivative (IV), which was reduced by sodium dithionite to the aminothioamide (III). The yield of thioamide was improved if isolation of the intermediate (IV) was omitted.

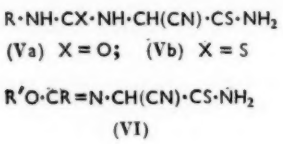
The aminothioamide (III) with cyanic acid, thiocyanic acid, and α-naphthyl isocyanate gave the ureas (Va; R = H or α-naphthyl) and the thiourea (Vb; R = H), whose behaviour with cyclising agents was complex and will not be discussed here.

The thioamide (III) with ethyl acetimidate gave the glyoxaline (Ib; R = Me, R′ = H). Initial attempts to prepare the linear imidate (VI; R = Me, R′ = Et) by reaction of the thioamide with ethyl acetimidate hydrochloride in water gave a compound which is regarded as the aminothiazole (VII; R = Me) since it could be diazotised and coupled with an alkaline solution of β-naphthol to give a red dye. However, the thioamide and benzyl acetimidate hydrochloride in water readily gave the crystalline linear imidate (VI; R = Me, R′ = CH_2Ph). This reacted smoothly with methylamine, ethylamine, and cyclohexylamine to give the aminoglyoxalinethiocarboxyamides (Ib; R = Me, R′ = Me, Et, and cyclohexyl respectively). These may be converted into purines by methods similar to those used for the aminocarboxyamides. Thus the glyoxaline (Ib; R = R′ = Me) with formic acid and acetic anhydride gave the 5-formamido-derivative (VIII; R = R′ = Me) which with hot dilute aqueous potassium hydrogen carbonate gave 6-mercapto-8,9-dimethylpurine (IX; R = R′ = Me). It has been recorded [3] that amidines may be prepared from thiocarboxyamides by reaction with mercuric chloride and ammonia. An attempt to apply this reaction to compound (Ib; R = R′ = Me) led to the nitrile (Ic; R = R′ = Me). The reaction was simplified and a quantitative yield of the nitrile obtained by using methylamine instead of ammonia in this reaction, the greater solubility of methylamine hydrochloride in alcohol facilitating separation of chloride from the reaction product. An attempt was also made to extend this reaction to the preparation of aminomalononitrile from the thioamide (III). Desulphurisation readily occurred and the product was a highly pungent oil which may have been the required product but its characterisation has been prevented by its instability.

It was harder to prepare aminoglyoxaline thiocarboxyamides unsubstituted at position 2 by these methods. Reaction of the hydrochlorides of ethyl, benzyl, butyl, or isobutyl formimidate and of butyl and benzyl thioformimidate with the thioamide (III) gave no useful results. However, the thioamide (III) with isopentyl formimidate hydrochloride in methyl cyanide gave the aminothiazole (VII; R = H). The required derivative (VI; R = H, R′ = isopentyl) was finally obtained in ethereal solution by ether-extraction of a mixture of the thioamide (III) and isopentyl formimidate hydrochloride in water. The ether solution with ammonia and methylamine readily gave the glyoxalines (Ib; R = H, R′ = H and Me respectively). The former compound is a probable intermediate in a synthesis of 6-mercaptopurine involving as a first step the reaction of the

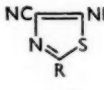
[2] Howard, U.S.P. 2,733,260/1956.
[3] Bernthsen, *Annalen*, 1876, **184**, 321; 1878, **192**, 1; Skinner and Neumann, *Chem. Rev.*, 1944, **35**, 351.

carboxyamide (Ia; R = R′ = H) with phosphoric sulphide.[4] The glyoxaline (Ib; R = H, R′ = Me) with formic acid and acetic anhydride gave a mixture of the 5-formamido-derivative (VIII; R = H, R′ = Me) and 6-mercapto-9-methylpurine (IX; R = H, R′ = Me). The mercaptopurine was also obtained by heating the formamide with aqueous

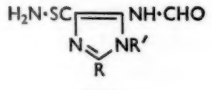


(Va) X = O; (Vb) X = S

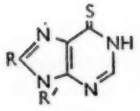
(VI)



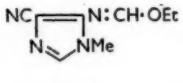
(VII)



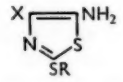
(VIII)



(IX)



(X)

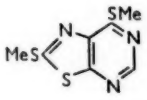


(XIa) X = $CS{\cdot}NH_2$

(XIb) X = $C(SMe){:}NH_2^+ MeSO_4^-$

(XIc) X = CN

(XId) X = $CO{\cdot}NH_2$



(XII)

potassium hydrogen carbonate. In addition, the corresponding amino-nitrile (Ic; R = H, R′ = Me) was readily obtained by desulphurisation of the thioamide (Ib; R = H, R′ = Me) with mercuric chloride and methylamine in ethanol. The amino-nitrile with ethyl orthoformate gave the ethoxymethylidene derivative (X) which with ammonia gave 9-methyladenine.

Purine analogues of potential value as metabolite antagonists include the thiazolo[5,41-*d*]-pyrimidines which have been prepared, *e.g.*, by completing the pyrimidine ring in an aminothiazolecarboxyamide [5] (XId; R = Me); the aminothiazole (XId; R = H) was obtained from aminocyanoacetamide and carbon disulphide.[6] In a similar manner the aminothiazole thiocarboxyamide (XIa; R = H) is formed quantitatively from the thioamide (III) and carbon disulphide. Methylation then gave a compound which from its elementary analysis and further reactions can only be the carboxythioimidate (XIb; R = Me). This salt with sodium hydroxide precipitated the amino-nitrile (XIc; R = Me) and with formic acid and acetic anhydride gave the thiazolopyrimidine (XII).

Experimental

α-Cyano-α-hydroxyiminothioacetamide.—To a solution of α-cyanothioacetamide [3] (36·5 g.) and sodium nitrite (25·6 g.) in water (1 l.) at ~10° was slowly added 10N-hydrochloric acid (36·5 ml.) in water (150 ml.) with cooling. At these concentrations, more intense cooling may result in precipitation of the thioamide. An amorphous precipitate separated and was filtered off through charcoal and asbestos. The filtrate was evaporated *in vacuo* to about 400 ml., then set aside at 0° overnight. The *hydroxyimino-derivative* (17 g.) which separated recrystallised from water as dark yellow-brown needles, m. p. 156° (decomp. from 140°) (Found: C, 28·15; H, 2·45; N, 31·85. $C_3H_3ON_3S$ requires C, 27·9; H, 2·3; N, 32·55%). A further quantity (19 g.) was obtained by extraction of the aqueous solution with ether. In this preparation the evaporation may be omitted, and a similar yield of the product isolated by extraction of the initial reaction solution with ether. The compound gave an intense blue colour with sodium hydroxide solution and ferrous sulphate.

α-Amino-α-cyanothioacetamide.—(*a*) The hydroxyimino-compound (19 g.) in water at 50°

[4] Hitchings and Elion, U.S.P. 2,756,228/1956.

[5] Cook, Heilbron, MacDonald, and Mahadevan, *J.*, 1949, 1064; Cook, Downer, and Heilbron, *J.*, 1949, 1069; Cook, Davies, Heilbron, and Thomas, *J.*, 1949, 1071.

[6] Cook, Heilbron, and Smith, *J.*, 1949, 1440.

was treated with solid sodium dithionite (57 g.); the solution became green and its temperature rose to 73°. The solution, when cooled, gave crystals (13·05 g.), which were extracted with hot ethyl acetate, leaving a considerable residue. Addition of light petroleum (b. p. 40—60°) to the filtrate precipitated *α-amino-α-cyanothioacetamide* (6·68 g.) which recrystallised from ethyl acetate or ethyl acetate–light petroleum (b. p. 40—60°) as buff-coloured plates, m. p. 110° (decomp.) (Found: C, 31·45; H, 4·35; N, 35·8. $C_3H_5N_3S$ requires C, 31·3; H, 4·4; N, 36·5%).

(*b*) 5N-Hydrochloric acid (164 ml.) was slowly added to a solution of α-cyanothioacetamide (82 g.) and sodium nitrite (58 g.) in water (800 ml.) at 25°. Sodium dithionite (285 g.) was then added. The cooled solution gave as under (*a*) the thioamide (33 g.), m. p. and mixed m. p. 110° (decomp.).

α-Acetamido-α-cyanothioacetamide.—The foregoing thioamide (0·57 g.) was warmed with acetic anhydride (2 ml.) for 5 min. The solution was evaporated *in vacuo* and the residue with water gave the *acetyl derivative* (0·5 g.), needles (from ethanol), m. p. 138° (Found: C, 38·5; H, 4·3; N, 26·2. $C_5H_7ON_3S$ requires C, 38·2; H, 4·5; N, 26·7%).

α-Cyano-α-ureidothioacetamide.—Potassium cyanate (0·8 g.) was added to α-amino-α-cyanothioacetamide (1·1 g.) in 50% acetic acid (10 ml.) at 0°. The *product* soon crystallised and was collected after 1 hr. and washed with ice-water. It separated from ethanol as prisms (1·8 g.), m. p. 196° (decomp. from 180°) (Found: C, 30·55; H, 3·65; N, 35·4. $C_4H_6ON_4S$ requires C, 30·4; H, 3·8; N, 35·45%).

N-α-(Cyanothiocarbamoylmethyl)-α-N′-α-naphthylurea.—α-Amino-α-cyanothioacetamide (0·57 g.) in warm ethyl acetate (15 ml.) with α-naphthyl isocyanate (0·85 g.) gave after 2 hr. a crystalline precipitate which was collected next morning. The *urea* (1·39 g.) recrystallised from aqueous methanol as needles, m. p. 203° (decomp.) (Found: C, 58·9; H, 4·2; N, 19·7. $C_{14}H_{12}ON_4S$ requires C, 59·15; H, 4·25; N, 20·3%). A solution of the urea (0·35 g.) in methanol (2·6 ml.) containing sodium (0·026 g.) was boiled under reflux for 1·5 hr., then evaporated to a gum. This largely dissolved in water (5 ml.), leaving a small amount of crystals, m. p. 80° (decomp.). The filtrate was acidified with a little dilute acetic acid to precipitate a solid which was soluble in excess of acid. This substance (0·15 g.) separated from ethanol as needles, m. p. 286° (decomp. from 230°) (Found: C, 59·25; H, 4·45; N, 16·6%). The same substance was obtained when the methanolic sodium methoxide was replaced by triethylamine in ethanol.

α-Cyano-N-α-thioureidothioacetamide.—α-Amino-α-cyanothioacetamide (2·85 g.) in water (5⁰ ml.) with potassium thiocyanate (2·4 g.) and 10N-hydrochloric acid (2·5 ml.) gave, after 2 days, a precipitate of the *thioureide hydrate* (2·1 g.). This separated from water as pale yellow needles, m. p. >300° (with preliminary darkening) (Found: C, 25·15; H, 4·3; N, 28·9. $C_4H_6N_4S_2,H_2O$ requires C, 25·0; H, 4·2; N, 29·1%). The compound was soluble in dilute sodium hydroxide solution and recovered by acidification. It gave no colour with ferric chloride solution.

5-Amino-2-methylglyoxaline-4-thiocarboxyamide.—α-Amino-α-cyanothioacetamide (0·58 g.) was added to methanolic ethyl acetimidate prepared from ethyl acetimidate hydrochloride (0·62 g.) in methanol (10 ml.) and sodium (0·55 g.) in methanol (3 ml.). The solution was boiled under reflux for 10 min., cooled, and treated with methanolic picric acid. The *glyoxalinepicrate methanolate* (0·75 g.) separated from methanol as yellow needles, m. p. 206—208° (decomp.) (Found: C, 34·75; H, 3·75; N, 22·85. $C_5H_8N_4S,C_6H_3O_7N_3,CH_4O$ requires C, 34·5; H, 3·6; N, 23·5%).

5-Amino-4-cyano-2-methylthiazole.—α-Amino-α-cyanothioacetamide (0·5 g.), ethyl acetimidate hydrochloride (1·2 g.), and water (1 ml.) were gently warmed together for 5 min. The cooled solution precipitated a little ammonium chloride which was removed. The filtrate then quickly deposited the *thiazole*. This separated from ethanol as needles (0·2 g.), m. p. 272° (decomp.) (Found: C, 43·65; H, 3·6; N, 30·1. $C_5H_5N_3S$ requires C, 43·5; H, 3·6; N, 30·2%), and could be diazotised and then coupled with alkaline β-naphthol to give a red colour. The same compound was formed when the reaction was carried out in dry methanol.

Benzyl N-(α-cyano-α-thiocarbamoylmethyl)acetimidate.—α-Amino-α-cyanothioacetamide (4 g.) and benzyl acetimidate hydrochloride (9·2 g.) were shaken with water (10 ml.) for a few minutes, crystals being soon deposited. More water (10 ml.) was added and the solid collected and washed with water and a little ice-cold ethanol. The *acetimidate* (4 g.) separated from ethyl acetate–light petroleum (b. p. 40—60°) as needles, m. p. 88° (Found: C, 58·2; H, 5·3; N, 16·75. $C_{12}H_{13}ON_3S$ requires C, 58·3; H, 5·3; N, 17·0%).

5-Amino-1,2-dimethylglyoxaline-4-thiocarboxyamide.—A suspension of the foregoing imidate

(0·5 g.) in methanol (5 ml.) with 33% ethanolic methylamine (0·3 ml.) soon gave a clear solution which quickly precipitated the *glyoxaline* (0·21 g.), plates (from methanol), m. p. 244—247° (decomp.) (Found: C, 42·6; H, 5·85; N, 33·0. $C_6H_{10}N_4S$ requires C, 42·35; H, 5·9; N, 32·95%). The compound when diazotised and coupled with an alkaline solution of β-naphthol gave a deep magneta-coloured dye. Addition of methanolic picric acid to the filtrate from the above reaction gave the *glyoxaline picrate* (0·05 g.), needles (from ethanol), m. p. 236—237° (decomp. from 210°) (Found: C, 36·15; H, 3·45; N, 24·45. $C_6H_{10}N_4S,C_6H_3O_7N_3$ requires C, 36·1; H, 3·3; N, 24·55%).

5-Amino-1-ethyl-2-methylglyoxaline-4-thiocarboxyamide.—The foregoing imidate (0·5 g.) under ethanol (5 ml.) with 20% ethanolic ethylamine precipitated the *glyoxaline* (0·23 g.) which recrystallised from ethanol as needles, m. p. 224—226° (decomp.) (Found: C, 45·85; H, 6·65; N, 30·35. $C_7H_{12}N_4S$ requires C, 45·65; H, 6·55; N, 30·45%), giving a deep red colour when diazotised and coupled with β-naphthol in alkaline solution.

5-Amino-1-cyclohexyl-2-methylglyoxaline-4-thiocarboxyamide.—The above imidate (0·25 g.) under ethanol (2 ml.) was gently warmed with cyclohexylamine (0·125 ml.) for a few minutes, to give a clear red solution whence the *glyoxaline* (0·035 g.), prisms (from ethanol), m. p. 278—280° (decomp.), soon separated (Found: C, 55·1; H, 7·55; N, 22·95. $C_{11}H_{19}N_4S$ requires C, 55·5; H, 7·6; N, 23·5%).

6-Mercapto-8,9-dimethylpurine.—5-Amino-1,2-dimethylglyoxaline-4-thiocarboxyamide (0·25 g.) was heated on a water-bath for 1 hr. with formic acid (2 ml.) and acetic anhydride (2 ml.). The solution was evaporated *in vacuo* and the residue stirred with methanol to leave a solid. *5-Formamido-1,2-dimethylglyoxaline-4-thiocarboxyamide* (0·25 g.) separated from methanol as needles, m. p. 256—257° (decomp.) (Found: C, 42·3; H, 4·8; N, 28·5. $C_7H_{10}ON_4S$ requires C, 42·4; H, 5·1; N, 28·3%). The formamide (0·25 g.) was heated on a water-bath for 2 hr. with potassium hydrogen carbonate (0·5 g.) in water (30 ml.). The solution was then evaporated to about 5 ml. and acidified with acetic acid to precipitate *6-mercapto-8,9-dimethylpurine* (0·17 g.) which separated from ethanol as hydrated rods, m. p. 250° (decomp.) (Found: C, 44·8; H, 5·2; N, 29·5. $C_7H_8N_4S,\frac{1}{2}H_2O$ requires C, 44·4; H, 4·8; N, 29·6%).

5-Amino-4-cyano-1,2-dimethylglyoxaline.—5-Amino-1,2-dimethylglyoxaline-4-thiocarboxyamide (1·65 g.) in methanol (200 ml.) and 33% ethanolic methylamine (5 ml.) with a solution of mercuric chloride (2·7 g.) in methanol (30 ml.) produced an immediate precipitate of mercuric sulphide. After a few minutes this was filtered off and washed with a little hot ethanol. The filtrate was evaporated to a crystalline residue which was washed with a little ethanol. The *glyoxaline* (1·3 g.) separated from ethanol as needles, m. p. 242° (Found: C, 52·95; H, 5·85; N, 41·3. $C_6H_8N_4$ requires C, 52·9; H, 5·95; N, 41·25%), giving a deep red colour when diazotised and coupled with an alkaline solution of β-naphthol. The *glyoxaline picrate* separated from ethanol as needles, m. p. 218° (decomp.) (Found: C, 39·6; H, 2·95; N, 27·2. $C_6H_8N_4,C_6H_3O_7N_3$ requires C, 39·5; H, 3·05; N, 26·8%).

5-Amino-4-cyanothiazole.—Isopentyl formimidate hydrochloride (0·85 g.) was added to a solution of α-amino-α-cyanothioacetamide (0·56 g.) in dry methyl cyanide (10 ml.). A precipitate of ammonium chloride was removed by centrifugation, and the clear solution evaporated *in vacuo* to a semi-solid residue. This partly crystallised from water to give the *thiazole* (0·1 g.) as needles, m. p. 149—150° (Found: C, 38·45; H, 2·35; N, 32·65. $C_4H_3N_3S$ requires C, 38·4; H, 2·4; N, 33·6%).

5-Aminoglyoxaline-4-thiocarboxyamide.—A mixture of α-amino-α-cyanothioacetamide (1·1 g.), isopentyl formimidate hydrochloride (3 g.), and water (5 ml.) was extracted with ether (3 × 20 ml.). The combined extracts were filtered through magnesium sulphate, then treated with excess of ethanolic ammonia to give a red solution. This was evaporated *in vacuo* to a low volume to remove ammonia, then methanolic picric acid was added to give a crystalline precipitate of the hydrated *glyoxaline picrate* (0·7 g.), rods (from methanol), m. p. 240° (after decomp.) (Found: C, 29·8; H, 3·6; N, 24·85. $C_4H_6N_4S,C_6H_3O_7N_3,2H_2O$ requires C, 29·5; H, 3·2; N, 24·1%).

5-Amino-1-methylglyoxaline-4-thiocarboxyamide.—Isopentyl formimidate hydrochloride (6 g.) was shaken with a suspension of α-amino-α-cyanothioacetamide (2·3 g.) in water (10 ml.) and ether (30 ml.). The ether solution was separated and the aqueous phase extracted with further ether (4 × 20 ml.). 33% Ethanolic methylamine (5 ml.) was added to the combined solutions, a vivid blue colour being produced which quickly changed to purple and then red; in this way a red oil was precipitated which soon crystallised. The solvent was decanted and the solid

washed with ethanol which removed the colour. The *glyoxaline* (1·06 g.) separated from ethanol as prisms, m. p. 252° (decomp. with shrinking from 238°) (Found: C, 38·25; H, 4·9; N, 36·0. $C_5H_8N_4S$ requires C, 38·45; H, 5·15; N, 35·85%). The compound was readily soluble in dilute hydrochloric acid, and when diazotised and coupled with an alkaline solution of β-naphthol gave a magenta-coloured dye.

5-Amino-4-cyano-1-methylglyoxaline.—Solutions of the foregoing glyoxaline (0·27 g.) in hot ethanol (50 ml.) and 33% ethanolic methylamine (1 ml.), and of mercuric chloride (0·47 g.) in ethanol (5 ml.), were mixed. The mercuric sulphide was filtered off, and the filtrate evaporated *in vacuo*, leaving the *glyoxaline* (0·12 g.), needles (from water), m. p. 195—196° (Found: C, 49·0; H, 4·8; N, 46·3. $C_5H_6N_4$ requires C, 49·2; H, 4·9; N, 45·9%).

6-Mercapto-9-methylpurine.—5-Amino-1-methylglyoxaline-4-thiocarboxyamide (0·5 g.) was dissolved in formic acid (2 ml.) and acetic anhydride (2 ml.). When the initial reaction had subsided, the solution was heated on a water-bath for 20 min. then evaporated *in vacuo* to a mixture of syrup and solid, which completely solidified when treated with water. The product was dissolved in hot ethanol, leaving an insoluble solid (0·05 g.); the cooled filtrate gave *5-formamido-1-methylglyoxaline-4-thiocarboxyamide* (0·4 g.) which separated from ethanol as pale yellow needles, which melted at 148—150° (decomp.), and resolidified, and then had m. p. >300° (Found: C, 39·6; H, 4·3; N, 30·4. $C_6H_8ON_4S$ requires C, 39·1; H, 4·4; N, 30·45%). The insoluble fraction was dissolved in dilute aqueous ammonia, the solution clarified with charcoal, and the mixture filtered. Acidification of the filtrate with dilute acetic acid gave a precipitate of *6-mercapto-9-methylpurine*, m. p. >300° (Found: C, 43·2; H, 3·7; N, 34·05. $C_6H_6N_4S$ requires C, 43·4; H, 3·65; N, 33·75%).

Also, the foregoing formamide (0·07 g.) was boiled under reflux with 0·05N-potassium hydrogen carbonate (30 ml.) for 2 hr. The cooled solution was acidified with acetic acid to precipitate the mercaptopurine (0·05 g.), m. p. >300° (Found: C, 43·1; H, 3·9; N, 34·0%).

9-Methyladenine.—5-Amino-4-cyano-1-methylglyoxaline (0·2 g.) in ethyl orthoformate (5 ml.) was boiled under reflux for 2 hr., then evaporated *in vacuo* to a gum which solidified when rubbed with water. *4-Cyano-5-ethoxymethylideneamino-1-methylglyoxaline* (0·15 g.) separated from water as needles, m. p. 52° (Found: C, 53·8; H, 5·5; N, 31·35. $C_8H_{10}ON_4$ requires C, 53·95; H, 5·65; N, 31·45%). The ethoxy-compound (0·1 g.) was heated in a sealed tube with saturated ethanolic ammonia (2 ml.) for 1 hr. and the solution was then evaporated. The residual 9-methyladenine (0·05 g.) separated from an excess of methanol as prisms, m. p. 298—299° (Found: C, 48·15; H, 4·9; N, 46·45. Calc. for $C_6H_7N_5$: C, 48·3; H, 4·75; N, 46·95%).

5-Amino-2-mercaptothiazole-4-thiocarboxyamide.—A solution of α-amino-α-cyanothioacetamide (3 g.) in methanol (30 ml.) and carbon disulphide (8 ml.) was boiled under reflux for 30 min. The *thiazole* (3·65 g.) which separated was purified by dissolution in N-sodium hydroxide and precipitation with acetic acid; it formed pale yellow prisms, m. p. 210° (decomp.) (Found: C, 25·1; H, 2·5; N, 21·9. $C_4H_5N_3S_3$ requires C, 25·15; H, 2·65; N, 22·0%).

Methyl 5-Amino-2-methylthiothiazole-4-thiocarboxyamidate.—A solution of the preceding thiazole (2 g.) in N-sodium hydroxide (10 ml.) was shaken with dimethyl sulphate (3 ml.) for a few minutes. The *methylthiothiazolium methyl sulphate* (2·5 g.) which separated formed pale yellow needles, m. p. 105° (decomp. and resolidified), from ethanol (Found: C, 25·25; H, 4·15; N, 12·2. $C_6H_9N_3S_3,CH_4O_4S$ requires C, 25·35; H, 3·95; N, 12·7%).

5-Amino-4-cyano-2-methylthiothiazole.—The foregoing sulphate (1 g.) in water (20 ml.) with 2N-sodium hydroxide (3 ml.) gave a crystalline precipitate. The *cyanothiazole* (0·4 g.) crystallised from ethanol as cream-coloured prismatic rods, m. p. 146° (Found: C, 35·2; H, 2·8; N, 24·2. $C_5H_5N_3S_2$ requires C, 35·1; H, 2·9; N, 24·5%).

2,7-Di(methylthio)thiazolo[5,4-d]pyrimidine.—The foregoing thiazole sulphate (0·4 g.) was heated on a water-bath with formic acid (2 ml.) and acetic anhydride (2 ml.) for 30 min. The solution was evaporated *in vacuo* to a syrup which crystallised when rubbed with water. The *thiazolopyrimidine* (0·2 g.) separated from ethanol as needles, m. p. 120°, which retained ethanol (Found: C, 38·6; H, 3·85; N, 16·8. $C_7H_7N_3S_3,\frac{1}{2}C_2H_6O$ requires C, 38·1; N, 4·0; N, 16·65%).

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812. *Oxidations of Organic Compounds with Quinquevalent Vanadium. Part III.*[1] *The Oxidation of Cyclohexanol.**

By J. S. Littler and William A. Waters.

The oxidations of cyclohexanol and 1-deuterocyclohexanol by quinquevalent vanadium in sulphuric acid solutions are of the first order with respect to both [V^V] and the alcohols. The acidity dependence in perchloric acid solution is indicative of oxidation by the cation $\{V(OH)_2\}^{3+}$; in sulphuric acid the more active oxidant is $[VO(H_2O)SO_4]^+$ or a similar complex ion. Optical measurements indicate that in perchloric acid solution all alcohols combine rapidly and reversibly with quinquevalent vanadium to form reddish complexes of composition $\{ROH,V(OH)_3\}^{3+}$. The oxidations of cyclohexanol and 1-deuterocyclohexanol proceed *via* these complexes and, since there is a kinetic isotope effect, C–H (or C–D) bond fission is involved in the rate-determining step. Evidence for a radical mechanism is put forward and discussed.

In Part I[2] it was indicated that primary and secondary alcohols were oxidised by acid solutions of quinquevalent vanadium with formation of free radicals. We have now studied kinetically the oxidations of cyclohexanol and 1-deuterocyclohexanol by quinquevalent vanadium, using perchloric and sulphuric acid solutions, and have been better able to elucidate the natures of the oxidising species in these two solutions.

Results.—Table 1 shows that the rate of consumption of vanadium(v) is of first order with respect to alcohol concentration. In this and the remaining Tables k is the first-order rate constant determined graphically from plots of log [V^V] against time. Oxidations carried out in the presence of excess of the alcohol all give good first-order reaction plots with respect to [V^V] (the total concentration of all vanadium(v) species) for at least 50% of the reaction (cf. Part II[1]).

Table 1. *Order with respect to alcohol of the oxidation of cyclohexanol in aqueous sulphuric acid.*

[V^V] = 0·05N, [H_3O^+] = 3·5M, ionic strength = 3·6M.

[Alcohol] (M)	0·0417	0·1038	0·125	0·166	0·2076
10^4k (sec.$^{-1}$)	0·121	0·268	0·328	0·447	0·537
10^4k/[alcohol]	2·88	2·58	2·62	2·69	2·59

Mean value of k/[alcohol] = (2·65 ± 0·08) × 10^{-4} mole^{-1} sec.$^{-1}$.

Tables 2 and 3 show that in both perchloric and sulphuric acid the oxidation rate is linearly dependent on the hydrogen-ion concentration $C_{H_3O^+}$, provided that the ionic strength is held constant by the addition of a salt of the same acid.

Table 2. *Order with respect to hydrogen-ion concentration of the oxidation of cyclohexanol in aqueous perchloric acid.*

[V^V] = 0·05N, ionic strength = 6·0M.

$C_{H_3O^+}$ (M)	1·04	3·32	4·20	4·68	5·59
[Alcohol] (M)	0·104	0·104	0·083	0·083	0·104
10^4k	0·137	0·337	0·375	0·414	0·608
10^4k/[alcohol]	1·32	3·24	4·52	4·98	5·85
10^4k/[alcohol] . $C_{H_3O^+}$	1·26	0·98	1·07	1·06	1·05

Mean value of k/[alcohol] . $C_{H_3O^+}$ = (1·08 ± 0·09) × 10^{-4} mole^{-2} sec.$^{-1}$.

In order to investigate the nature of the deep red complex of vanadium(v) formed in sulphuric acid solutions,[2] oxidations were carried out in solutions of almost constant

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[1] Part II, Littler and Waters, *J.*, 1959, 3014.
[2] Littler and Waters, *J.*, 1959, 1299.

acidity and constant ionic strength in which perchlorate ions had been progressively replaced by bisulphate ions. Table 4 shows that until about two thirds of the perchlorate has been replaced the oxidation rate increases linearly with bisulphate concentration.

TABLE 3. *Order with respect to hydrogen-ion concentration of the oxidation of cyclohexanol in aqueous sulphuric acid.*

$[V^V] = 0{\cdot}05$N, $[HSO_4^-] = 6{\cdot}0$M, ionic strength = 6·0M, [alcohol] = 0·104M.

$C_{H_3O^+}$ (M)	2·7	4·3	5·9
10^4k	0·494	0·802	1·10
$10^5k/C_{H_3O^+}$	1·83	1·86	1·87

Mean value of $k/C_{H_3O^+} = (1{\cdot}85 \pm 0{\cdot}02) \times 10^{-5}$ mole^{-1} sec.$^{-1}$.

TABLE 4. *Effect of bisulphate ion on the oxidation of cyclohexanol in aqueous perchloric acid.*

$[V^V] = 0{\cdot}05$N, [alcohol] = 0·104M, ionic strength = 6·0M.

$[HSO_4^-]$ (M)	0	1·2	2·4	3·6	4·8	6·0
$[H_3O^+]$ (M)	5·6	5·65	5·7	5·8	5·85	5·9
10^4k	0·608	0·750	0·895	0·995	1·06	1·10
$10^5k/[H_3O^+] = 10^5k'$	1·09	1·33	1·57	1·72	1·81	1·87
$10^5(k' - k'_0)$	0	0·24	0·48	0·63	0·72	0·78
$10^6(k' - k'_0)/[HSO_4^-]$	—	2·0	2·0	1·9	1·5	1·3

Mean value $(k' - k'_0)/[HSO_4^-] = 2{\cdot}0 \times 10^{-6}$ mole^{-2} sec.$^{-1}$ in range 0—4M-H_2SO_4.

TABLE 5. *Effect of sodium perchlorate on the rate of oxidation in perchloric acid.*

$[V^V] = 0{\cdot}05$N, [alcohol] = 1·04M, $[H_3O^+] = 1{\cdot}04$M.

Ionic strength (M)	3·6	6
10^5k	0·34	1·37

Table 5 shows that the addition of sodium perchlorate increases the rate of oxidation in perchloric acid solution.

The addition of vinyl cyanide leads to the production of insoluble polymers that contain both carbonyl and hydroxyl groups, but the addition does not greatly affect the rate of oxidation. The reacting mixtures absorb some oxygen, but this has but slight effect on the rate of disappearance of quinquevalent vanadium (Table 6).

TABLE 6. *Effect of addition of vinyl cyanide and of oxygen on the rate of reduction of vanadium*(V).

$[V^V] = 0{\cdot}05$N, [alcohol] = 0·104M.

$[H_2SO_4] = 5{\cdot}9$M, ionic strength = 6·0M. $[HClO_4] = 3{\cdot}5$M, ionic strength = 3·6M.

Atmosphere	air	O_2	N_2	[Vinyl cyanide] (M)	0	0·31
10^4k	1·10	1·08	1·19	10^5k	2·7	2·8

Consecutive reactions occur after the initial attack. Adipic acid is eventually formed, in almost quantitative yield, with consumption of eight equivalents of vanadium(V). In contrast to cyclohexanone, which is rapidly oxidised, up to five days are needed to ensure the complete oxidation of cyclohexanol at 50° in 4·2M-sulphuric acid. This could indicate that a relatively resistant intermediate, such as cyclohexyl adipate,[3] may be formed. Under similar conditions diphenylmethanol was oxidised only to benzophenone; benzoic acid could not be detected.

Samples of 1-deuterocyclohexanol and cyclohexanol, prepared by the same method, have been oxidised under identical conditions in both perchloric and sulphuric acid solutions. Table 7 shows that there are kinetic isotope effects of moderate magnitude.

A red-brown solution is formed immediately on admixture of yellow acid solutions of

[3] Milas, *J. Amer. Chem. Soc.*, 1928, **50**, 493.

quinquevalent vanadium with all alcohols. With cyclohexanol and 1-deuterocyclohexanol this colour persists until it is obscured by the blue colour of the vanadium(IV) resulting from the oxidation of the alcohol. As this oxidation is very slow at room temperature it has been possible to investigate the relationship between the intensity of the reddish colour and the concentrations of acid, cyclohexanol, and quinquevalent vanadium (see

TABLE 7. *Isotope effects on the oxidation of cyclohexanol by vanadium*(V).

$[V^V] = 0{\cdot}05$, ionic strength = 6M, (*a*) $[H_2SO_4] = 5{\cdot}9$M, (*b*) $[HClO_4]_4 = 5{\cdot}59$M.

Isotope	[alcohol] (M)	10^4k	10^4k/[alcohol]	H/D rate ratio
(*a*) H	0·0857	0·932	10·88	4·5
D	0·0824	0·199	2·41	
(*b*) H	0·104	0·608	5·85	3·6
D	0·0824	0·133	1·61	

Experimental), and to establish that the intensity of the colour is proportional to the product $[H_3O^+][V^V]$[alcohol]. The colour is dependent on ionic strength; use of the deutero-alcohol makes no difference to its intensity.

Cyclohexyl orthovanadate $(C_6H_{11}\cdot O)_3VO$, which is stable to distillation under diminished pressure,[4,5] was prepared by the method of Prandtl and Hess.[4] It is not catalytically decomposed to vanadium(IV) in toluene solution by addition of the bases water, ammonia, or pyridine, or by anhydrous hydrogen chloride or acetic and chloroacetic acid, but the Lewis acids aluminium trichloride and boron trifluoride do promote formation of vanadium(IV). However all these acids and bases catalyse the reduction of the vanadate ester by ketones and olefins. Although t-butyl alcohol is not oxidised by vanadium(V), these catalysed oxidations could also be effected by t-butyl orthovanadate. The reduction of trialkyl orthovanadates in contact with moist air reported by Prandtl and Hess,[4] and the slow decomposition of these esters to vanadium(IV) compounds in storage, have been found to be photochemical decompositions. Prandtl and Hess reported that the isopropyl and the isopentyl ester are photosensitive; the phenomenon seems to be quite general.

DISCUSSION

(1) *Nature of the Reactive Oxidants.*—In Part II [1] the oxidation of ketones by acid vanadium(V) was ascribed to the cation $V(OH)_3^{2+}$ in perchloric acid solutions, and to a sulphate complex in sulphuric solutions. The form of the acid-dependence of the oxidation rate of cyclohexanol in perchloric acid is identical with that observed for the oxidation of cyclohexanone, and so can be ascribed to the same ions (eqns. 1). The kinetic data on

$$VO_2^+ + H_3O^+ \rightleftharpoons V(OH)_3^{2+}$$

$$ROH + V(OH)_3^{2+} \underset{\text{fast}}{\rightleftharpoons} [\text{complex}]^{3+} \xrightarrow[\text{slow}]{} \text{products} \quad \ldots\ldots (1)$$

bisulphate-dependence (Table 4) indicate that the transition state formed during oxidation by the sulphuric acid complex contains both hydrogen and bisulphate ions; the marked colour of sulphuric acid solutions of vanadium(V) indicates that this extra bisulphate ion is present in the red vanadium(V) species. The additional reactions (2) and (3) must therefore be occurring. Bobtelsky and Glasner [6] found that the oxidation of ethanol depended on the concentration of alcohol and of vanadium(V), but they did not explain the acid-dependence that they observed.

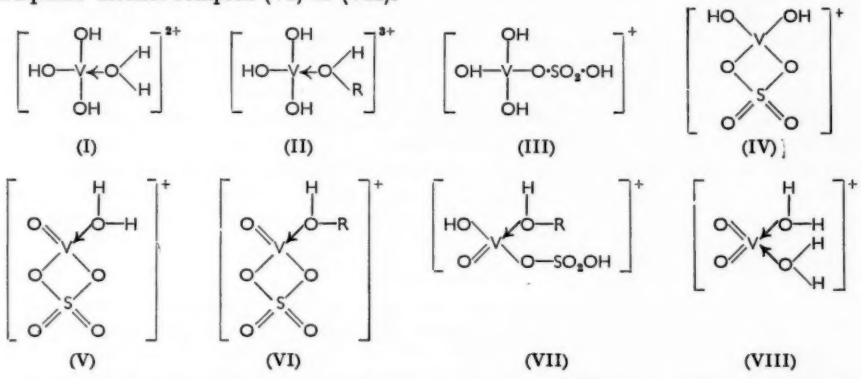
$$V(OH)_3^{2+} + HSO_4^- \underset{\text{fast}}{\rightleftharpoons} \{V(OH)_3HSO_4\}^+ \quad \ldots\ldots\ldots (2)$$

$$\{V(OH)_3HSO_4\}^+ + ROH \underset{\text{fast}}{\rightleftharpoons} [\text{complex}] \xrightarrow[\text{slow}]{} \text{products} \quad \ldots\ldots (3)$$

[4] Prandtl and Hess, *Z. anorg. Chem.*, 1913, **82**, 103.
[5] Funk, Weiss, and Zeising, *Z. anorg. Chem.*, 1958, **296**, 36.
[6] Bobtelsky and Glasner, *J. Amer. Chem. Soc.*, 1942, **64**, 1462.

Our spectrophotometric measurements in perchloric acid confirm the existence of a relatively stable alcohol complex, and indicate that it has the composition $\{ROH,V(OH)_3\}^{2+}$. A similar intensification of colour occurs immediately on mixing alcohols with sulphuric solutions of vanadium(v), so the bisulphate complex $\{ROH,V(OH)_3,HSO_4\}^+$ must also be formed rapidly. Similar complex formation was shown by Ardon to occur between cerium(IV) and alcohols.[7]

If these complexes are co-ordination compounds, in which vanadium(v) is tetrahedrally co-ordinated as in $VOCl_3$,[8] VO_4^{3-},[9] VO_3^-,[10] V_2O_5,[11] and orthoesters $(RO)_3VO$, then the yellow doubly charged cation of vanadium(v) may be (I) (a hydrated entity), the alcohol complex in perchloric acid (II), the bisulphate complex (III), (IV), or (V), and the bisulphate–alcohol complex (VI) or (VII).



(I) (II) (III) (IV)

(V) (VI) (VII) (VIII)

The immediate formation of the alcohol complexes suggests that a direct substitution of a co-ordinated R–OH for a co-ordinated H–OH may occur, possibly with inversion about the vanadium centre, rather than a displacement by RO of an OH. Again V–O–R bonds are very easily hydrolysed, and so under these aqueous conditions an ester is not likely to remain formed. The simple substitution of $-O{\cdot}SO_2{\cdot}OH$ for –OH (III) would not be expected to produce the marked difference in colour between perchlorate and sulphuric solutions of vanadium(v); formulæ in which the sulphate group is a chelating ligand [(IV) and (V)] can explain this difference. Chelating sulphate groups are present in the ceric complexes $(CeSO_4)^{2+}$, $Ce(SO_4)_2$, and $\{Ce(SO_4)_3\}^{2-}$.[12] The structure (V) is to be preferred to (IV) since it more easily indicates the ease of replacement of H_2O by ROH. Similarly the ion VO_2^+, which is probably not linear,[13] may be weakly hydrated as in (VIII), which is of the type of (V) and (VI).

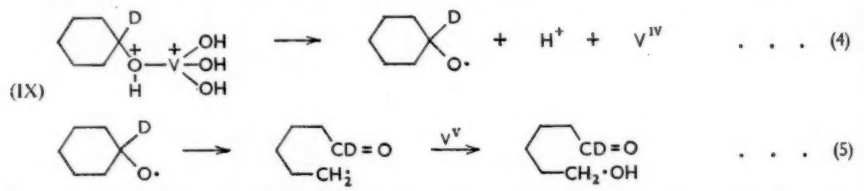
Further evidence for the existence of the ion $V{:}O(OH_2)SO_4^+$ comes from the work of Lanford and Kiehl,[14] who isolated the solid $V_2O_5,4SO_3,4H_2O$ from 18M-sulphuric acid. Ramsey, Colichman, and Pack[15] interpreted this compound as $\{V(OH)_2^{3+}\}_2(SO_4^{2-})_3,H_3O^+,HSO_4^-$ but it could be equally well written as $\{VO{\cdot}OH_2{\cdot}SO_4\}^+HSO_4^-,\frac{1}{2}H_2O$, *i.e.*, a salt of structure (V). It does not contain sufficient water to be a derivative of the non-chelated ion (III). Rates of oxidations involving active ions such as $V(OH)_2^{3+}$ or VO^{3+} would have depended on $[C_{H_3O^+}]^2$ and not on $[C_{H_3O^+}][HSO_4^-]$. The lack of any departure from first-order dependence on $C_{H_3O^+}$ in either

[7] Ardon, *J.*, 1957, 1811.
[8] Palmer, *J. Amer. Chem. Soc.*, 1938, **60**, 2360.
[9] Mulligan and Vernon, *J. Phys. Chem.*, 1952, **56**, 145.
[10] Wells, "Structural Inorganic Chemistry," 2nd edn., Oxford Univ. Press, 1950, p. 499.
[11] Keletaar, *Z. Krist.*, 1939, **95**, 9; Byström, Wilhelmi, and Brotzen, *Acta Chem. Scand.*, 1950, **4**, 1119.
[12] Hardwick and Robertson, *Canad. J. Chem.*, 1951, **29**, 828.
[13] LaSalle and Cobble, *J. Phys. Chem.*, 1955, **59**, 519.
[14] Lanford and Kiehl, *J. Amer. Chem. Soc.*, 1940, **62**, 895.
[15] Ramsey, Colichman, and Pack, *J. Amer. Chem. Soc.*, 1946, **68**, 1695.

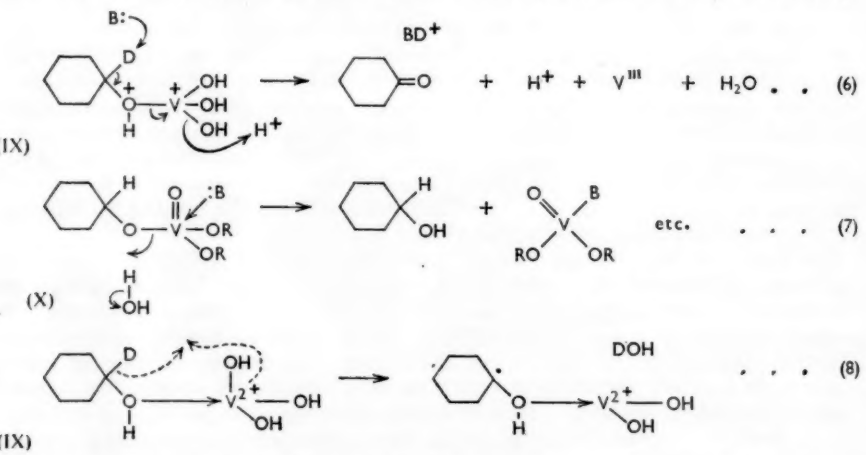
sulphuric or perchloric acid solutions shows that at no time were the complex-forming equilibria (1,2,3) displaced sufficiently to the right to invalidate the assumption that $[VO_2^+] \equiv$ [Total of all species of V^V].

(2) *Mechanism of Oxidation of Primary and Secondary Alcohols.*—The catalysis of the polymerisation of vinyl cyanide shows that organic free radicals are formed during the oxidation of alcohols. Whilst some of these may be formed in the oxidation of subsequently formed ketones or aldehydes, isolated dry polymers from cyclohexanol had an absorption band at 3400 cm.$^{-1}$ which indicated that they contain hydroxyl groups. Since the polymers from cyclohexanone do not exhibit this absorption it can be inferred that hydroxyl-containing radicals are formed in the initial steps of the alcohol oxidation. The relative resistance to oxidation of alcohols compared with ketones [2] is consistent with the behaviour of other one-electron oxidisers.[16]

The isotope effect observed indicates that the C–H or C–D bond of the carbinol group is involved in the rate-determining step of the oxidation. If oxidation proceeds by O–V bond fission to leave an alkoxy-radical and vanadium(IV), then the C–D bond would not be involved (eqn. 4). Fission and oxidation (eqn. 5) would then be expected to follow.[17] This mechanism would not explain the resistance of t-butyl alcohol to oxidation or the absence of any benzoic acid among the products of oxidation of diphenylmethanol.



An acid–base catalysed two-electron redistribution (6) such as that proposed by Westheimer [18] for the oxidation of alcohols by chromium(VI) would account for the isotope



effect but is not consistent with resistance of the orthovanadate esters to acid–base-catalysed reduction, or the formation of $R_2C{\cdot}OH$ radicals. The hydrolysis of orthovanadate esters can be represented as in (7), in which electron movement is of a different type from that in (6).

[16] Waters, *Quart. Rev.*, 1958, **12**, 277.
[17] Hawkins, *J.*, 1950, 2801.
[18] Westheimer, *Chem. Rev.*, 1949, **45**, 419.

A mechanism which fits all the evidence is a cyclic one-electron decomposition of the complex (8) in which bond formation between D from C–D and OH from V–OH participates in the rate-determining stage. The difference between the isotope effects in perchloric and sulphuric acid can be accounted for by the difference between the H, or D, abstracting species;[19] in one case $\{V(OH)_3\}^{2+}$ and in the other $(VOSO_4)^+$. This radical decomposition (8) of the complex (IX) would not be acid- or base-catalysed and the resistance of ortho-esters (X) may be due to the inability of the vanadium atom to acquire a sufficiently large positive charge to pull off the hydrogen atom in non-aqueous solution, except when co-ordinated (*e.g.*, XI) with an extremely strong electron-withdrawing group such as $AlCl_3$ or BF_3.

(9)

Either the bisulphate ligand is sufficiently strongly electron-withdrawing in comparison with the groups it replaces to overcome the effect of the reduced overall charge of the complex or the concentration of the bisulphate complex (VI) is larger than that of (II). The photochemical decomposition of orthovanadate esters (X) including t-butyl orthovanadate must proceed by a mechanism different from (8).

Experimental

Materials.—Vanadium(v) solutions were made up as described in Part II.

Cyclohexanol (commercial, 1% maximum ketone), after being washed with ferrous sulphate and water, was distilled under nitrogen over 2,4-dinitrophenylhydrazine up a short fractionating column. After removal of any water as the azeotrope, the alcohol was collected at 159·5°. After a further fractionation the alcohol showed no absorption at 1700 cm.$^{-1}$ (C=O bond).

1-*Deuterocyclohexanol.*—Lithium aluminium deuteride (0·80 g.) (Metal Hydrides Inc., 97·5%) and 5 ml. of pure (see Part II) cyclohexanone in dry ether were refluxed for ½ hr. Excess of deuteride was decomposed with wet ether, and dilute hydrochloric acid was added. The ethereal layer was separated and the aqueous layer extracted three times with further quantities of ether. The combined extracts were dried ($MgSO_4$). Under diminished pressure the ether was removed and the residue was distilled over quicklime into a receiver protected from moisture ($CaCl_2$ tube). A sample of the protio-compound, made in the same way from lithium aluminium hydride, was used in the comparative experiments. The rate of oxidation of this sample did not differ by more than 2% from the rate calculated from the experiments with the bulk cyclohexanol purified as described above. The spectra of the alcohols prepared by reduction of cyclohexanone showed no carbonyl absorption at 1700 cm.$^{-1}$. The deuterium compound had a moderately strong C–D absorption at 2100 cm.$^{-1}$, and its spectrum differed considerably from that of the protio-compound in the 750—1400 cm.$^{-1}$ region.

Kinetic measurements, polymerisations, and studies of oxygen uptake were carried out at 50·0° ± 0·2° as described in Part II.

Spectrophotometric measurements were carried out on a Hilger " Spekker " absorptiometer using " spectrum violet " gelatine filters (601) to isolate the wavelength region 3900 Å to 4700 Å, in which the alcohol complex absorbed more strongly than the other vanadium(v) ions present.

Solutions of the complex in perchloric acid were compared with the relevant solutions of vanadium(v) in perchloric acid. The absorption was found to be proportional to: (1) the concentration of alcohol (0·0—0·14M) at constant acidity (5·5M), ionic strength (5·8M), and $[V^V]$ (0·2N); (2) $[H_3O]^+$ (0—4·5M) at constant concentration of alcohol (0·104M) and vanadium(v) (0·05N), and at constant ionic strength (6·0M); (3) $[V^V]$ (0—0·15N) at constant ionic strength (3·6M), acidity, and alcohol concentration (0·104M) when balanced against corresponding solutions containing no alcohol. Also, when the acidity and ionic strength were increased together [as in (2), but ionic strength 1·2M—6M] the increase in absorption was greater than

[19] Swain, Stivers, Reuwer, and Schaad, *J. Amer. Chem. Soc.*, 1958, **80**, 5885.

XUM

when acidity alone was increased. Replacement of cyclohexanol by 1-deuterocyclohexanol did not alter the absorption. The absorption of vanadium(v) in alcohol-free solutions did not alter with acidity.

Complete Oxidation of Cyclohexanol.—10 ml. of alcohol solution (0·415M) and 200 ml. of 0·2N-vanadium(v) solution in 4·4M-sulphuric acid were mixed and left at 50° for 5 days. Titration of the solution showed that each mole of cyclohexanol had reduced 7·97 equivalents of vanadium(v) (Calc. for $C_6H_{11}\cdot OH + 4O \longrightarrow (CH_2)_4(CO_2H)_2$: 8 equiv.). Ether-extraction yielded the expected quantity of adipic acid, m. p. and mixed m. p. 151°.

One of us (J. S. L.) thanks the Salters' Company for a Scholarship.

DYSON PERRINS LABORATORY, SOUTH PARKS ROAD, OXFORD. [*Received, May 19th*, 1959.]

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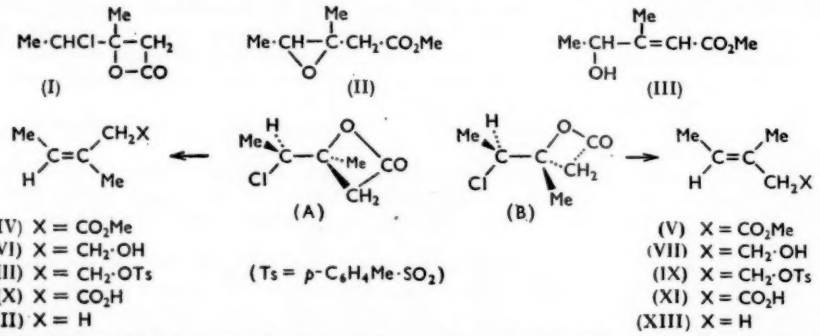
813. *Stereoselective Reaction of Keten with 3-Chlorobutan-2-one; Geometry of the 3-Methylpent-3-enoic Acids.*

By (MRS.) R. H. CORNFORTH.

The reaction of keten with 3-chlorobutan-2-one is shown to give, in the ratio 2 : 3, two stereoisomers of 4-chloro-3-methylpentano-3-lactone. These have been isolated and converted into *cis*- and *trans*-3-methylpent-3-enoic acids and the corresponding alcohols. Methyl 3-methylpent-3-enoate prepared by Favorski re-arrangement of 3,4-dibromo-3-methylpentan-2-one is shown to be 75% *trans*. Two other chloro-β-lactones are described.

GRIGNARD reagents and lithium alkyls have been shown to add stereoselectively to aliphatic α-chloro-carbonyl compounds [1]; thus R^4X reacts with $R^1R^2ClC\cdot COR^3$ to give a chlorohydrin having a preponderance of molecules where R^4 is *anti* to the larger of the two groups R^1 and R^2 when the chlorine and hydroxyl groups are *anti* to each other. When R^1 and R^2 are hydrogen and alkyl, respectively, stereospecific reduction of the derived iodohydrin gives a mixture of olefins in which 70% has R^4 *trans* to R^2 when the starting material is an α-chloro-aldehyde, and 80—85% when it is an α-chloro-ketone. Sodium borohydride reduction is also 80—85% stereoselective in the expected sense. We were interested in applying this stereoselectivity in the reactions of α-chloro-ketones to a synthesis of optically active mevalonic acid (3,5-dihydroxy-3-methylpentanoic acid) starting from a compound



$RO\cdot CH_2\cdot CHCl\cdot COMe$ of known absolute configuration; a highly stereoselective reaction of an α-chloro-ketone with keten in the presence of boron trifluoride would have been admirable for this purpose.

To test the stereoselectivity of the reaction, 3-chlorobutan-2-one was treated with keten

[1] Cornforth, Cornforth, and Mathew, *J.*, 1959, 112.

in the presence of boron trifluoride: this gave a crystalline mixture of 4-chloro-3-methylpentano-3-lactones (I) which was converted into a mixture of methyl *cis*- and *trans*-3,4-epoxy-3-methylpentanoate (II) by cautious treatment with less than one equivalent of sodium methoxide in methanol; if the reaction mixture is allowed to become alkaline re-arrangement [2] readily occurs to methyl 4-hydroxy-3-methylpent-2-enoate (III). This reaction is naturally interpreted as an opening of the β-lactone ring by attack of methoxide ion on the carbonyl group; formation of the epoxide from the resulting chlorohydrin anion occurs in a second step, with inversion at the halogen-bearing carbon. The iodohydrins from the mixture of epoxy-esters were reduced by stannous chloride–phosphorus oxychloride–pyridine to a mixture of methyl *cis*- and *trans*-3-methylpent-3-enoate (IV and V); reduction with lithium aluminium hydride gave the alcohols (VI and VII), the toluene-*p*-sulphonates of which (VIII and IX) were further reduced by lithium aluminium hydride to a mixture of *cis*- and *trans*-3-methylpent-2-enes (XII and XIII). This mixture was shown, by comparison of infrared spectra,[1] to contain about 60% of the *trans*-form. Thus the reaction of 3-chlorobutan-2-one with keten is much less stereoselective than with organometallic reagents and the degree of selectivity was not sufficient for the proposed synthesis of mevalonic acid. Possibly keten is effectively smaller than an organometallic reagent in solution and therefore less subject to steric hindrance; an organometallic reagent presumably reacts as an ether solvate, but this is not necessarily true of keten.

The literature on the 3-methylpent-3-enoic acids (X and XI) presents a rather unsatisfactory picture. Kon, Linstead, and Wright [3] studied the isomeric αβ- and βγ-unsaturated acids obtained by dehydration of 3-hydroxy-3-methylpentanoic acid and its ester; the acids were separated by partial esterification. After equilibration of the αβ-unsaturated acids with alkali, partial esterification gave an ester which on hydrolysis gave an acid of m. p. 1°; this was assumed to be pure 3-methylpent-*cis*-3-enoic acid. On the other hand, when the product from dehydration of ethyl 3-hydroxy-3-methylpentanoate with phosphoric oxide was hydrolysed and partially esterified, the resulting βγ-unsaturated ester could be hydrolysed to give, on crystallisation, an acid of m. p. 35°; this was assigned the *trans*-configuration. No derivatives were described and the assignments of configuration were purely provisional. Now Wagner [4] claimed to have obtained methyl 3-methyl-*trans*-pent-3-enoate stereochemically pure by Favorski re-arrangement of 3,4-dibromo-3-methylpentan-2-one obtained from 3-methylpent-3-en-2-one of unspecified geometry; he did not isolate the parent acid but made derivatives (amide, anilide, and *p*-toluidide) which he compared with derivatives of "*cis*"- and "*trans*"-3-methylpent-3-enoic acids prepared according to Kon, Linstead, and Wright; he accepted their provisional assignment of structure as fact. Undoubtedly the anilide and *p*-toluidide were identical with those from the acid of m. p. 35° accepted as *trans*, and thus Wagner's ester is likely to consist predominantly of this form; but the isolation of pure re-crystallised derivatives, unless in quantitative yield, does not indicate stereochemical homogeneity of the starting material. The weight of further evidence is in favour of the *trans*-configuration for the acid, m. p. 35°, as assigned by Kon, Linstead, and Wright. Thus, Ansell and Gadsby [5] reduced Wagner's ester to the corresponding alcohol and converted this into its homologue, 4-methylhex-4-en-1-ol; from this specimen and from the hexenol obtained by scission with sodium of 3-chlorotetrahydro-2,3-dimethylpyran the same α-napthylurethane was obtained by reaction with α-naphthyl isocyanate and recrystallisation of the products. This correlation was considered proof of the stereochemical homogeneity of the ring-scisson product. A *trans*-configuration for the latter was supported by theoretical consideration of the mechanism of ring scisson and by the fact that tiglic and angelic acid can both be converted *via* the derived allylic bromides into a hexenol in which, as judged by preparation of derivatives,

[2] Rambaud, *Compt. rend.*, 1945, **220**, 742.
[3] Kon, Linstead, and Wright, *J.*, 1934, 599.
[4] Wagner, *J. Amer. Chem. Soc.*, 1949, **71**, 3214.
[5] Ansell and Gadsby, *J.*, 1958, 3388.

the alcohol from the scission was the major component: in the reaction sequence used, the thermodynamically more stable *trans*-configuration would be expected to predominate. Also, Loftfield [6] has put forward a convincing stereospecific mechanism for the Favorski re-arrangement; since one would expect Wagner's starting material, 3-methylpent-3-en-2-one, to be predominantly *trans*, the derived methyl 3-methylpent-3-enoate should also be predominantly *trans*. This is now proved to be so; methyl 3-methylpent-3-enoate prepared according to Wagner was hydrolysed to the corresponding acid, which was liquid at room temperature and therefore could not be pure "*trans*"-acid, m. p. 35°; the acid was reduced by lithium aluminium hydride, and the methanesulphonate of the 3-methylpent-3-en-1-ol further reduced by lithium aluminium hydride to 3-methylpent-2-ene, which was shown by comparison of infrared spectra to be about 75% *trans*. Thus Wagner's ester and Ansell and Gadsby's 3-methylpent-*trans*-3-en-1-ol (and the corresponding *cis*-isomer which they obtained by a series of reactions designed to invert the geometry of the double bond) must also be about 75% stereochemically pure (equal yields being assumed from both isomers in the various transformations).

There seems little ground for the assumption that the acid of m. p. 1° is stereochemically pure; Wagner assumed that it was and described three derivatives (amide, anilide, and *p*-toluidide), only the last of which gave any substantial depression on admixture with the corresponding derivative of the *trans*-acid or of the Favorski re-arrangement product.

The mixture of 4-chloro-3-methylpentano-3-lactones, if it could be separated into its stereoisomers, offered a means of preparing stereochemically pure samples of *cis*- and *trans*-3-methylpent-3-enoic acids and the corresponding alcohols. By chromatography on silica gel two crystalline forms (A), m. p. 71—72°, and (B) m. p. 56—57°, were obtained, the latter being present in larger amount. The melting point of the original mixture (36—38°) was that of a 2 : 3 mixture of A and B (see Table 2). The infrared spectra of these two mixtures were also very similar. Since the mixture of lactones can be converted into a mixture of 3-methylpent-2-enes containing 60% of the *trans*-isomer it may be assumed that (A) is the form giving rise to the *cis*- and (B) that giving rise to the *trans*-olefin. Lactones (A) and (B) were converted respectively into the *cis*- and *trans*-isomers of methyl 3,4-epoxy-3-methylpentanoate and of methyl 3-methylpent-3-enoate; the infrared spectrum of a mixture of 2 parts of the *cis*- and 3 parts of the *trans*-3-methylpent-3-enoate was also very similar to that of the unsaturated ester from the original lactone mixture. Hydrolysis of the *cis*- and *trans*-esters gave 3-methylpent-*cis*-3-enoic, m. p. 14·5—15·5°, and 3-methylpent-*trans*-3-enoic acid, m. p. 35°. Melting points of these acids and their derivatives are assembled in Table 1. Examination of the data shows that the assignment of the *trans*-configuration to the acid, m. p. 35°, by Kon, Linstead, and Wright was correct but that the

TABLE 1. *3-Methylpent-3-enoic acids and derivatives.*

Source of acid	M. p.	Amide, m. p.		Anilide, m. p.		*p*-Toluidide, m. p.	
Pure *cis* from chloro-lactone A	14·5—15·5°	138—139°	mixed 125—127	111—112·5°	mixed 96—98	100—101°	mixed 75
Pure *trans* from chloro-lactone B	35	136—137		98—99		91—92	
"*trans*" prepd. by Wagner according to Kon *et al.*	35	—		100—101	mixed 97—98	91·5—92·5	mixed 70
"*cis*" prepd. by Wagner according to Kon *et al.*	1 (Kon *et al.*)	126—127	mixed 127—130	99—100		100·5—101·5	
Favorski re-arr. product (Wagner)	—	130—131		99—100		91—92	mixed 70

acid, m. p. 1°, was obviously a mixture. Since Wagner succeeded in isolating one pure *cis*-derivative (the *p*-toluidide) from this mixture it is presumably richer in the *cis*- than the *trans*-acid. Wagner's re-arrangement product furnished pure *trans*-anilide and -*p*-toluidide

[6] Loftfield, *J. Amer. Chem. Soc.*, 1951, **73**, 4707.

but the amide was not pure *trans*. The composition of Wagner's ester (75% *trans*) was also confirmed by comparison of the spectrum of the derived alcohol with those of mixtures of pure *cis*- and *trans*-alcohol (VI) and (VII). The pure alcohols were prepared by reduction of the esters (IV) and (V) with lithium aluminium hydride; their α-naphthylurethanes had higher melting points than those prepared by Ansell and Gadsby from the alcohols derived from Wagner's ester.

In drawing conclusions about the stereochemical composition of the mixture of chloro-lactones (I) and of Wagner's ester from the composition of the final olefin mixture it has been assumed that the two isomers give equal yields in the various transformations. This assumption seems reasonable, and after the separation of the chloro-lactone mixture into the two pure forms (A) and (B) supporting evidence was available from mixed m. p.'s and infrared spectra of mixtures of (A) and (B) and also from infrared spectra of mixtures of the derived *cis*- and *trans*-unsaturated esters and alcohols. The assignment of *cis*- and *trans*-configurations rests ultimately on the composition of the derived 3-methylpent-2-enes. The hypothesis that the proportions of *cis*- and *trans*-isomers in, *e.g.*, Wagner's ester could have become reversed in transformation to the methylpentenes requires too great a difference in yields to be seriously entertained.

Because of the unexpected crystallinity of the 4-chloro-3-methylpentano-3-lactones, the β-lactones from chloroacetone and 3-chloropentanone were also examined; that from chloroacetone was crystalline, m. p. 25°, but the mixture from 3-chloropentan-2-one was liquid and could not be separated into crystalline isomers by chromatography. Pyrolysis of 4-chloro-3-methylpentano-3-lactone at 150—160° gave a good yield of 3-chloro-2-methylbut-1-ene, but none of these chloro-β-lactones was decarboxylated in water, as was β-methylbutyro-β-lactone.[7]

Experimental

4-Chloro-3-methylpentano-3-lactone; Isomers A and B.—A solution of 3-chlorobutan-2-one (21·3 g.) in dry ether (25 c.c.) was cooled to −15°, boron trifluoride–ether complex (0·6 c.c.) was added, and keten (slightly more than 0·2 mole) was passed in; the internal temperature rose to 5—10°. The mixture was diluted with more ether, washed with saturated sodium hydrogen carbonate solution (40 c.c.) and saturated sodium chloride solution, dried ($MgSO_4$), and evaporated at low pressure. The residue crystallised from dry ether (80 c.c.) at −70°, to give 25 g. (84%) of colourless *4-chloro-3-methylpentano-3-lactone*, m. p. 36—38° (Found: C, 48·5; H, 6·4; Cl, 23·9. $C_6H_9O_2Cl$ requires C, 48·5; H, 6·1; Cl, 23·9%). A few crystals left on a watch-glass evaporated overnight. The chloro-lactone (2 g.) was pyrolysed at 150—160° to give 1·3 g. of distillate; redistillation gave 3-chloro-2-methylbut-1-ene (1·0 g., 76%), b. p. 92—94°, n_D^{22} 1·4310 (Found: C, 57·1; H, 8·6. Calc. for C_5H_9OCl: C, 57·4; H, 8·6%). Burgin *et al.*[8] give b. p. 93·8°, n_D^{20} 1·4304.

The above mixture of stereoisomers (10 g.) in cyclohexane (300 c.c.) was added to a column of silica gel (B.D.H.) (500 g.) and eluted with cyclohexane–benzene (50 : 50), the eluate being collected in 100 c.c. portions. Fractions 1—13 gave on evaporation 3·6 g. (a), m. p. 53—56°; thereafter the m. p. dropped to 36—39° (fraction 20), then rose to 59—67° (fraction 27). The solvent was changed to benzene after fraction 30. Fractions 27—33 gave on evaporation 1·2 g. (b), m. p. 60—65°, fractions 34—37 gave 1·4 g. (c), m. p. 65—70°, and fractions 38—40 gave 0·25 g. (d), m. p. 67—70°. Total recovery from the column was 8·75 g. Material (a), recrystallised from cyclohexane (20 c.c.), gave 3·2 g. of lactone, m. p. 56—57° (Found: C, 48·5; H, 6·1%); materials (b), (c), and (d), recrystallised from cyclohexane, gave 2·7 g., of lactone, m. p. 70—71°, raised to 71—72° by a second recrystallisation (Found: C, 48·5; H, 6·2%). Three recrystallisations of fractions 14—19 and 21—26 gave respectively 0·5 g., m. p. 55—56°, and 0·6 g., m. p. 70—71°. Since conversion into 3-methylpent-2-ene, described below, gave a mixture predominantly *trans*, it may be assumed that the isomer, m. p. 56—57°, has structure (B) and the isomer, m. p. 71—72°, structure (A). The infrared spectrum of a 2 : 3 mixture of (A)

[7] Gresham, Jansen, Shaver, and Beears, *ibid.*, 1954, **76**, 486.
[8] Burgin, Engs, Groll, and Hearne, *Ind. Eng. Chem.*, 1939, **31**, 1414.

and (B) was very similar to that of the original mixture. The annexed Table of mixed m. p.s also indicates that the original mixture is composed of (A) and (B) in the ratio 2 : 3.

TABLE 2. *M. p.s of mixtures of (A), m. p. 71—72°, and (B), m. p. 56—57°.*

Ratio A : B	1 : 3	3 : 7	1 : 2	2 : 3	1 : 1	2 : 1
M. p.	39—45°	37—42°	37—42°	36—39°	40—49°	50—60°

Methyl 3,4-*Epoxy*-3-*methylpentanoate* (*Mixture of Geometrical Isomers*).—A solution of the mixture of chloro-β-lactones (10 g.) in dry methanol (20 c.c.) was heated in a water-bath at 55—60°. Evaporation (to avoid excessive volumes) was encouraged by rapid stirring during titration with 2N-sodium methoxide (Cresol Red as indicator); the reaction, at first very rapid, gradually became more sluggish and care was taken to prevent the solution remaining even faintly alkaline for any length of time. The titration was stopped short of the theoretical (32·7 instead of 33·7 c.c.; time 45 min.). The solution was filtered from sodium chloride and evaporated; the residue was taken up in ether, filtered, recovered by evaporation, and distilled, giving *methyl* 3,4-*epoxy*-3-*methylpentanoate* (6·6 g., 64%), b. p. 72—78° (mostly 74—75°)/16 mm. (Found: C, 58·0; H, 8·3. $C_7H_{12}O_3$ requires C, 58·3; H, 8·3%), and 1·9 g. of material, b. p. 110—120°/16 mm. (Found: C, 58·6; H, 8·4%). The higher-boiling fraction is isomeric with the epoxy-ester; infrared and ultraviolet absorption spectra [$\nu_{max.}$ 3400 (OH) and 1720 cm.$^{-1}$ (ester); $\lambda_{max.}$ (in EtOH) 2180 Å (ε 13,500)] confirmed its structure as *methyl* 4-*hydroxy*-3-*methylpent*-2-*enoate*. In some experiments, when the reaction mixture was allowed to become too alkaline, this product predominated.

Methyl 3-*Methylpent*-3-*enoate* (*Mixture of Geometrical Isomers*).—The epoxy-ester mixture (29·5 g.) was added to sodium iodide (60 g.) and sodium acetate (6 g.) in propionic acid (240 c.c.) and acetic acid (80 c.c.) at −20°. After 2 hr. the mixture was warmed to 0°, another 20 g. of sodium iodide were added, and the mixture was kept at 0° for a further 2 hr. It was then poured (with stirring) into ether and excess of aqueous sodium hydrogen carbonate. The ether was washed with aqueous sodium hydrogen sulphite and water, dried ($MgSO_4$), and evaporated at low pressure. The iodohydrin (51 g.) was added to anhydrous stannous chloride (52 g.) in pyridine (200 c.c.) at 0° and treated cautiously with phosphoryl chloride (15 c.c.) in pyridine (50 c.c.). The mixture was allowed to warm to a maximum temperature of 50° during solidification. After 3 hr. ether was added, the mixture was filtered, and the residue washed with ether. The ethereal solution was cooled in ice-water and made just acid to Methyl Orange with dilute hydrochloric acid; after separation, the ether layer was treated with water and small quantities of iodine until the brown colour persisted, then washed with sodium thiosulphate–sodium carbonate solution and dried ($MgSO_4$), and the ether was distilled off through a fractionating column. The residue was distilled, to give methyl 3-methylpent-3-enoate (17·5 g., 67%), b. p. 49—52°/16 mm. (Found: C, 65·7; H, 9·8. Calc. for $C_7H_{12}O_2$: C, 65·7; H, 9·4%).

3-*Methylpent*-2-*ene* (*Mixture of Geometrical Isomers*).—Methyl 3-methylpent-3-enoate (17 g.), obtained as above, was reduced with lithium aluminium hydride (8 g.) in ether (220 c.c.), essentially as described by Ansell and Gadsby,[5] to give 3-methylpent-3-en-1-ol (10·6 g., 80%), b. p. 58—60°/16 mm., n_D^{20} 1·4470. The toluene-*p*-sulphonate (11·6 g.), prepared according to Ansell and Gadsby's directions, in dry peroxide-free dibutyl ether (20 c.c.) was added dropwise during 1 hr. to lithium aluminium hydride (2 g.) in the same solvent (70 c.c.) with stirring; the temperature rose to 34—36°. After the addition the mixture was heated and stirred for 2·5 hr. at 45°, cooled in ice-water, and decomposed by water (10 c.c.). Next day the mixture was filtered, the residue washed with dibutyl ether, and the filtrate (which was neutral to litmus) distilled through a Widmer column. The distillate (6·75 g., b. p. ≯138°) gave a slight reaction with dinitrophenylhydrazine and was therefore shaken with a strong solution of semicarbazide acetate for 30 min., washed with water, aqueous sodium hydrogen carbonate, and water again, dried (KOH), and distilled from a flask with an indented neck. The distillate up to 90° (2·4 g.) was left over calcium chloride overnight (to remove any butyl alcohol) and distilled over sodium; 3-methylpent-2-ene (1·92 g.; b. p. 68—73°) was thus obtained. The infrared spectrum was almost identical with that of a 2 : 3 mixture of *cis*- and *trans*-3-methylpent-2-ene.[1]

3-*Methylpent*-trans-3-*enoic Acid*.—The chloro-lactone (B) (6·5 g.) was converted as described above into *methyl* trans-3,4-*epoxy*-3-*methylpentanoate* (4·9 g., 78%), b. p. 69—72°/16 mm., n_D^{21} 1·4230 (Found: C, 57·9; H. 8·5%). Reduction of the derived iodohydrin (8·4 g. from 4·5 g.) gave *methyl* 3-*methylpent*-trans-3-*enoate* (3·2 g.), b. p. 48—49°/16 mm., n_D^{21} 1·4318 (Found: C, 65·8; H, 9·6%). Hydrolysis of the ester (500 mg.) with 2N-sodium hydroxide (3 c.c.) and

methanol (3 c.c.) at room temperature for several days gave 3-methylpent-*trans*-3-enoic acid (442 mg.; m. p. 34—35°); recrystallisation from light petroleum (b. p. 40—60°) at 2° did not raise the m. p. The *amide* was prepared from the ester and saturated methanolic ammonia at 36° (5 weeks); it formed plates, m. p. 136—137° raised to 137—138° on one recrystallisation from benzene (Found: C, 63·8; H, 10·0. $C_6H_{11}ON$ requires C, 63·7; H, 9·7%). The anilide, prepared from the acid and aniline with dicyclohexylcarbodi-imide, had m. p. 98—99°, not raised by recrystallisation from light petroleum (b. p. 60—80°). The *p*-toluidide prepared in a similar manner had m. p. 89—90°, raised to 91—92° after two crystallisations from light petroleum (b. p. 60—80°). M. p.s recorded in the literature are given in Table 1.

3-*Methylpent*-trans-3-*en*-1-*ol*.—Reduction of methyl 3-methylpent-*trans*-3-enoate (1·3 g.) by lithium aluminium hydride gave 3-methylpent-*trans*-3-en-1-ol (0·91 g.), b. p. 58°/15 mm., n_D^{21} 1·4480 (Found: C, 71·6; H, 12·1. Calc. for $C_6H_{12}O$: C, 71·9; H, 12·1%); the α-naphthylurethane, recrystallised from light petroleum (b. p. 60—80°), had m. p. 81—82: (Found: C, 75·7; H, 7·1. Calc. for $C_{17}H_{19}O_2N$: C, 75·8; H, 7·1%). Ansell and Gadsby [5] gave m. p. 78—78·5° for the α-napthylurethane of material shown below to be only 75% *trans*.

3-*Methylpent*-cis-3-*enoic Acid*.—The chloro-lactone (A) (9·6 g.) gave *methyl* cis-3,4-*epoxy*-3-*methylpentanoate* (5·8 g.), b. p. 65—67°/16 mm., n_D^{21} 1·4230 (Found: C, 58·1; H, 8·5%). Reduction of the derived iodohydrin (9·1 g. from 5 g.) gave *methyl* 3-*methylpent*-cis-3-*enoate*, (3·5 g.; b. p. 43—44°/16 mm., n_D^{21} 1·4298 (Found: C, 65·9; H, 9·4%). Hydrolysis of the ester (500 mg.) gave liquid 3-*methylpent*-cis-3-*enoic acid* (425 mg.), which distilled at about 40°/0·005 mm. and then had m. p. 14·5—15·5°, not raised by recrystallisation from ether at −70° (Found: C, 69·9; H, 9·0. $C_6H_{10}O_2$ required C, 63·1; H, 8·8%). The *amide* formed plates (from benzene), m. p. 138—139° (Found: N, 12·0. $C_6H_{11}ON$ requires N, 12·3%). The *anilide*, recrystallised from light petroleum (b. p. 60—80°) had m. p. 111—112·5° (Found: C, 76·0; H, 8·1. $C_{12}H_{15}ON$ requires C, 76·2; H, 7·9%). The *p*-toluidide had m. p. 100—101° after recrystallisation from light petroleum (b. p. 60—80°) (Found: C, 76·6; H, 8·3. Calc. for $C_{13}H_{17}ON$: C, 76·8; H, 8·4%). Earlier data and m. p.'s for mixtures are given in Table 1.

The infrared spectrum of methyl 3-methylpent-3-enoate prepared from the mixture of chloro-lactones corresponded to that of a mixture of pure *cis*- and *trans*-esters in the proportion 2 : 3.

3-*Methylpent*-cis-3-*en*-1-*ol*.—Reduction of methyl 3-methylpent-*cis*-3-enoate (1·7 g.) with lithium aluminium hydride gave 3-methylpent-*cis*-3-en-1-ol (1·1 g.), b. p. 56—57°/16 mm., n_D^{21} 1·4466 (Found: C, 71·8; H, 12·0%). The α-naphthylurethane had m. p. 111—112° after recrystallisation from light petroleum (b. p. 60—80°). Ansell and Gadsby [5] gave m. p. 105° for the α-napthylurethane of the " *cis* "-alcohol derived from the " *trans* "-alcohol now shown to be only 75% *trans*.

Determination of the Stereochemical Composition of Wagner's Methyl 3-*Methylpent*-trans-3-*enoate*.—Methyl 3-methylpent-3-enoate prepared by Wagner's method [4] was hydrolysed at room temperature with a slight excess of 2N-methanolic potassium hydroxide diluted with an equal volume of water. The 3-methylpent-3-enoic acid obtained distilled at 50—52°/0·05 mm. and its ultraviolet absorption spectrum showed that it contained no αβ-isomer. It solidified at 0° but was liquid at room temperature. Reduction of the acid (12 g.) by lithium aluminium hydride in ether gave 3-methylpent-3-en-1-ol (7·7 g.), b. p. 58—62° (mostly 58—59°)/16 mm., n_D^{20} 1·4466. The alcohol (3·5 g.) was added slowly, with stirring, to methanesulphonyl chloride (8 g.; two-fold excess) and pyridine (7·6 g.) at 5° at a rate to keep the temperature at 10—12°; the mixture was stirred without cooling for 1 hr. longer. Next day it was poured on ice and extracted with ether; the ether was washed with dilute sulphuric acid, sodium hydrogen carbonate solution, and water, dried, and evaporated. The *methanesulphonate* (4·7 g.) distilled at 84—86°/0·03 mm. (Found: C, 46·8; H, 7·8. $C_7H_{14}O_3S$ requires C, 47·2; H, 7·9%); it was reduced, as described above for the toluene-*p*-sulphonate, by means of lithium aluminium hydride (1 g.) in dibutyl ether (35 c.c.). The distillate boiling up to 138° (3·9 g.) smelt very strongly of thiol; it was therefore washed repeatedly with sodium hydroxide and water and dried. Distillation from a flask with an indented neck gave 1·04 g. of b. p. up to 90°; this was redistilled over sodium to give 0·8 g. of 3-methylpent-2-ene, b. p. 67—70°. The infrared spectrum corresponded to that of a mixture of 3-methylpent-2-enes containing 75% of the *trans*-isomer. The infrared spectrum of the intermediate alcohol also corresponded with that of a 3 : 1 mixture of *trans*- and *cis*-alcohols.

γ-*Chloro*-β-*methylbutyro*-β-*lactone*.—Chloroacetone (20·75 g.) in dry ether (18 c.c.) was cooled

to −15°, boron trifluoride–ether complex (0·6 c.c.) added, and a slight excess of keten passed in. The mixture was worked up as described above. The residue after evaporation of the ether did not crystallise; on distillation it gave lactone (22·9 g.), b. p. 36—42°/0·003 mm. Recrystallisation from dry ether (50 c.c.) at −70° gave *γ-chloro-β-methylbutyro-β-lactone* (18·5 g.), m. p. 24—25° (Found: C, 44·4; H, 5·1. $C_5H_7O_2Cl$ requires C, 44·6; H. 5·2%).

4-Chloro-3-methylhexano-3-lactone.—From 3-chloropentan-2-one (14·85 g.), treated as for chloroacetone (above), a product was obtained which was heated to 40°/0·01 mm. to remove unchanged ketone. The residue (9·4 g.) did not crystallise. Chromatography of a portion, as described for 4-chloro-3-methylpentano-3-lactone, did not give crystalline fractions. The eluate was distilled to give *4-chloro-3-methylhexano-3-lactone*, b. p. 45—50°/0·001 mm. (Found: C, 52·0; H, 6·6. $C_7H_{11}O_2Cl$ requires C, 51·7; H, 6·8%). This is presumably a mixture of stereoisomers.

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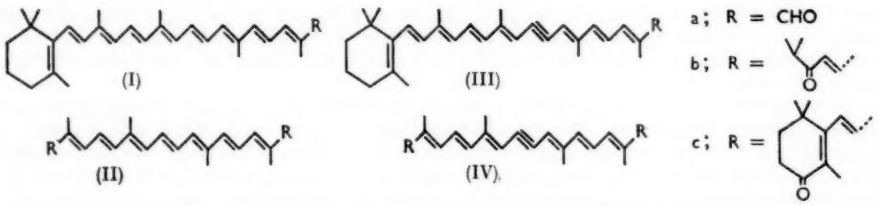
814. *Carotenoids and Related Compounds. Part VIII.* Novel Syntheses of Echinenone and Canthaxanthin.*

By M. AKHTAR and B. C. L. WEEDON.

Syntheses of echinenone and canthaxanthin, by use of Robinson's Mannich base reaction, are described.

IN Part VII unambiguous total syntheses of echinenone and canthaxanthin were reported. Recently details of an alternative route to the latter were given by Isler *et al.*[1] The present paper describes convenient new syntheses of both carotenoids, and records the first applications in this field of Robinson's Mannich base method for the formation of cyclohexenone rings.



Condensation of apo-2-carotenal (Ia) [2] and crocetindial (IIa) [3] with isopropyl methyl ketone in the presence of alcoholic potassium hydroxide gave the decaenone (Ib) and nonaenedione (IIb) [4] in 80—85% yields. Reaction of these ketones with a large excess of 1-diethylaminopentan-3-one methiodide and alcoholic potassium ethoxide then gave echinenone (Ic) and canthaxanthin (IIc) directly in 27 and 12% yields, respectively.

It seemed of interest to examine the substitution of the polyene aldehydes by their acetylenic analogues (IIIa) [2] and (IVa) [3] in the above syntheses. Condensation with isopropyl methyl ketone gave the ketones (IIIb) and (IVb) in 90 and 70% yields, respectively. When treated with the Mannich base these ketones gave 15,15′-dehydroechinenone (IIIc) and 15,15′-dehydrocanthaxanthin (IVc) in *ca.* 60 and 40% yield,

* Part VII, *J.*, 1958, 3986.

[1] Zeller, Bader, Lindlar, Montavon, Müller, Rüegg, Ryser, Saucy, Schaeren, Schwieter, Stricker, Tamm, Zürcher, and Isler, *Helv. Chim. Acta*, 1959, **42**, 841.

[2] Rüegg, Montavon, Ryser, Saucy, Schwieter, and Isler, *Helv. Chim. Acta*, 1959, **42**, 854.

[3] Isler, Gutman, Lindlar, Montavon, Rüegg, Ryser, and Zeller, *Helv. Chim. Acta*, 1956, **39**, 463.

[4] Warren and Weedon, *J.*, 1958, 3972.

respectively. The marked superiority of the acetylenic, compared with the polyenic, intermediates in the Robinson reaction is surprising. Condensation of the ketone (IIIb) with ethyl vinyl ketone also gave dehydroechinenone (45%).

Reduction of dehydroechinenone over a Lindlar catalyst gave (85%) " central-*cis* " echinenone which yielded " all-*trans* " echinenone (Ic) on irradiation in the presence of a trace of iodine. The similar conversion of 15,15'-dehydrocanthaxanthin into canthaxanthin (IIc) has already been described by Isler *et al.*[1] The dehydrocanthaxanthin prepared in the present studies was identical in all respects with a sample kindly supplied by Dr. O. Isler.

The spectral properties of most of the compounds mentioned above are summarised in the Tables. The acetylenic compounds exhibited maximal light absorption in the

TABLE 1. *Light absorption of polyene aldehydes and ketones in benzene.*
(Max in mμ; ε × 10^{-3} in parentheses.)

Polyenes		*Monoacetylenes*	
Ia	469 (85)	IIIa	440 (71)
Ib	480 (118)	IIIb	454 (99)
Ic [a]	472 (115)	IIIc	445 (90)
IIa	470 (85) 443 (92) 422 (62)	IVa	445 (62) 417 (73)
IIb [b]	518 (103) 483 (115) 458 (78)	IVb	485 (85) 454 (98)
IIc	480 (118)	IVc	448 (80)

[a] Cf. Warren and Weedon, *J.*, 1958, 3986. [b] Warren and Weedon, *J.*, 1958, 3972.

visible region at wavelengths *ca.* 25—30 mμ shorter than their polyene counterparts, and " central-*cis* " echinenone displayed a pronounced " *cis*-peak." The carbonyl bands were only poorly resolved in the infrared spectra of the isopropyl ketones. As expected (cf. ref. 4) the cyclohexenones exhibited well-defined carbonyl bands at lower frequencies and of greater intensity. The acetylenic compounds were characterised by weak C≡C

TABLE 2. *Infrared light absorption of polyene aldehydes and ketones.*
(Chloroform solutions or, where indicated, potassium bromide disc. Frequencies in cm.$^{-1}$ with an indication of relative intensity; ε for carbonyl bands in parentheses.)

Compd.	Conj. C≡C stretch.	Conj. C=O stretch.	Conj. C=C stretching region			CH out-of-plane deformation region of conj. *trans*-CH=CH		
Ia†		1639 vs	1600 s	1563 m		1000 m	967 ms	
IIIa	2141 m	1658 vs	1597 s	1570 m		1000 m	990 *	961 m
Ib		1678 * 1658 s 1645 s		1577 vs 1504 s	1550 vs	996 *	971 vs	957 m
IIIb	2151 m	1672 ms (~100) 1650 s 1639 s		1587 * 1550 vs	1575 s 1515 *	981 *	975 s	963 *
Ic		1655 s (440)	1613 w	1577 w	1558 w		971 vs	
IIIc	2151 w	1653 s (470)	1613 w		1563 w		972 s	957 *
IIa		1667 vs	1605 s	1570 s		998 s	966 s	
IVa	2151 w	1667 vs	1605 s	1587 s		1000 s	988 *	959 s
IIb [a]		1675 s (~250) 1656 m 1645 m		1585 †s	1545 vs†	980 s†	970 s†	
IVb	2155 w	1672 s (~200) 1656 s 1645 s		1587 s	1555 vs	981 s	987 m	962 s
IIc [b]		1651 vs (940)	1608 w†	1581 m†	1555 s†,		966 s†	
IVc	2155 w	1653 vs (920)	1613 w	1587 *	1563 m		972 s	958 *

* Shoulder. † KBr disc. w, weak; m, medium; s, strong; vs, very strong.
[a] Warren and Weedon, *J.*, 1958, 3972. [b] Warren and Weedon, *J.*, 1958, 3986.

stretching frequencies at *ca.* 2155 cm.$^{-1}$, and by an absorption at *ca.* 960 cm.$^{-1}$ which occurred either as a separate maximum or as a shoulder on the main band in the CH out-of-plane deformation region of conjugated *trans*-CH=CH-bonds. Differences between the spectra of the polyenes and their monoacetylenic analogues were also apparent in the C=C stretching region.

Experimental

As far as possible all operations were carried out in an inert atmosphere, usually of nitrogen. Alumina for chromatography was pretreated as described by Cheeseman *et al.*[5] and was Grade IV on the Brockmann and Schodder [6] activity scale.

Those m. p.s determined on a Kofler block are corrected.

1-*Diethylaminopentan*-3-*one*.—Reaction of propionyl chloride (300 g.) in chloroform (1 l.) with ethylene in the presence of aluminium chloride (453 g.) gave 1-chloropentan-3-one (160 g.), b. p. 40°/1 mm., n_D^{23} 1·4360 (McMahon *et al.*[7] give b. p. 33°/2·5 mm., n_D^{20} 1·4361).

Treatment of the chloro-ketone (160 g.) in ether (400 c.c.) with diethylamine (192 g.) in ether (500 c.c.) yielded 1-diethylaminopentan-3-one (160 g.), b. p. 98—99°/50 mm., n_D^{22} 1·4345 (Adamson *et al.*[8] give b. p. 84°/13 mm., n_D^{15} 1·4368). Reaction of the amino-ketone with an equal amount of methyl iodide [9] afforded a methiodide as a hygroscopic solid which was used without purification.

2,6,10,15,19-*Pentamethyl*-21-(2,6,6-*trimethylcyclohex*-1-*enyl*)*heneicosa*-4,6,8,10,12,14,16,18,20-*nonaen*-3-*one* (Ib).—A solution of β-apo-2-carotenal (60 mg.) and 3-methylbutan-2-one (1 c.c.) in 5% ethanolic potassium hydroxide (4 c.c.) was kept at 20° for 12 hr. The product (59 mg.) which had crystallised from the reaction medium had m. p. 156—158°. Crystallisation from benzene–methanol gave the *ketone*, m. p. 158—159° (Kofler block), 159—161·5° (evacuated sealed capillary tube) (Found: C, 86·6; H, 9·85. $C_{35}H_{48}O$ requires C, 86·7; H, 10·0%).

Echinenone (Ic).—A solution of the preceding ketone (40 mg.) in benzene (5 c.c.) was added to one of potassium ethoxide (from 250 mg. of potassium) in ethanol (5 c.c.). 1-Diethylaminopentan-3-one methiodide (2·0 g.) in alcohol (10 c.c.) was added and the mixture ($\lambda_{max.}$ 480 mμ) was stirred and boiled under reflux for 2½ hr. Potassium ethoxide (from 250 mg. of potassium) in ethanol (10 c.c.) was added and the mixture boiled overnight. The mixture ($\lambda_{max.}$ 470 mμ) was cooled and poured into dilute hydrochloric acid. Extraction of the product with light petroleum (b. p. 60—80°), chromatography from benzene–light petroleum (b. p. 60—80°) on alumina, collection of the main band, evaporation, and crystallisation of the residue from pentane–chloroform, gave echinenone (11 mg.), m. p. and mixed m. p. 178—179° (evacuated capillary tube) (Petracek and Zechmeister [10] give m. p. 175—178°). A chromatogram of a mixture with an authentic specimen showed no separation.

2,6,10,15,19,23-*Hexamethyltetracosa*-4,6,8,10,12,14,16,18,20-*nonaene*-3,22-*dione* (IIb).—A mixture of crocetindial (1·0 g.), 3-methylbutan-2-one (60 c.c.), and 5% ethanolic potassium hydroxide (80 c.c.) was shaken occasionally and kept at 20° for 24 hr. The product (1·2 g.) which had crystallised had m. p. 180—182°. Recrystallisation from benzene–light petroleum (b. p. 60—80°) gave the nonaenedione (1·0 g.) as purple plates, m. p. 184—186° (Warren and Weedon [4] give m. p. 187°).

Canthaxanthin (IIc).—A solution of the preceding nonaenedione (86 mg.) in benzene (7 c.c.) was added to one of potassium ethoxide (from 315 mg. of potassium) in ethanol (7 c.c.), and the mixture was stirred at 20° for 1 hr. 1-Diethylaminopentan-3-one methiodide (2·5 g.) in alcohol (12 c.c.) was added, and the mixture was boiled and diluted with ethanol (35 c.c.). The resulting homogeneous solution was boiled under reflux for 6·5 hr. Potassium ethoxide (from 270 mg. of potassium) in ethanol (6 c.c.) was added and boiling was continued for another hour. The mixture, which no longer showed an ultraviolet light absorption maximum with $\lambda > 500$ mμ, was cooled and poured into dilute hydrochloric acid. Extraction of the product with benzene, and chromatography from benzene–light petroleum (b. p. 60—80°) on alumina gave three red bands. Collection of the middle band, evaporation, and crystallisation of the residue from pentane–chloroform gave canthaxanthin (12 mg.), m. p. and mixed m. p. 211—212° (evacuated capillary tube) (Petracek and Zechmeister [10] give m. p. 213—214°). A chromatogram of a mixture with an authentic specimen revealed no separation.

Substitution of potassium hydroxide for potassium ethoxide in the above reaction had no ill-effect.

[5] Cheeseman, Heilbron, Jones, and Weedon, *J.*, 1949, 3120.
[6] Brockmann and Schodder, *Ber.*, 1941, **74**, 73.
[7] McMahon, Roper, Utermohlen, Hasek, Harris, and Brant, *J. Amer. Chem. Soc.*, 1948, **70**, 2971.
[8] Adamson, McQuillin, Robinson, and Simonsen, *J.*, 1937, 1576.
[9] Wilds and Shunk, *J. Amer. Chem. Soc.*, 1943, **65**, 469.
[10] Petracek and Zechmeister, *J. Amer. Chem. Soc.*, 1956, **78**, 1427.

2,6,10,15,19-*Pentamethyl*-21-(2,6,6-*trimethylcyclohex*-1-*enyl*)*heneicosa*-4,6,8,10,14,16,18,20-*octaen*-12-*yn*-3-*one* (IIIb).—A solution of 8,9-dehydro-β-apo-2-carotenal (300 mg.) and 3-methylbutan-2-one (3 c.c.) in 5% ethanolic potassium hydroxide (12 c.c.) was kept at 20° for 14 hr. The product (315 mg.) which had crystallised had m. p. 151—153°; crystallisation from benzene–methanol gave the *ketone* as deep-orange plates, m. p. 153—154·5° (Kofler block) (Found: C, 87·45; H, 9·6. $C_{35}H_{46}O$ requires C, 87·1; H, 9·6%).

15,15′-*Dehydroechinenone* (IIIc).—(i) A solution of the preceding ketone (43 mg.) in benzene (3 c.c.) was added to one of potassium ethoxide (from 150 mg. of potassium) in ethanol (3 c.c.). 1-Diethylaminopentan-3-one methiodide (1·2 g.) in ethanol (6 c.c.) was added and the mixture ($\lambda_{max.}$ 454 mμ) was stirred and boiled under reflux for 1½ hr. Potassium ethoxide (from 100 mg. of potassium) in ethanol (5 c.c.) was added, and the mixture was boiled for 18 hr. The reaction mixture ($\lambda_{max.}$ 442—445 mμ) was cooled and poured into dilute hydrochloric acid. Extraction of the product with benzene–light petroleum (b. p. 60—80°), chromatography from benzene–light petroleum (b. p. 60—80°) on alumina, collection of the main band, evaporation, and crystallisation from light petroleum (b. p. 40—60°) gave a solid (27·5 mg.), m. p. 164—166°. Recrystallisation from the same solvent yielded *dehydroechinenone*, as deep-orange plates, m. p. 168—171° (Kofler block) (Found: C, 87·65; H, 9·4. $C_{40}H_{52}O$ requires C, 87·55; H, 9·55%).

(ii) A solution of the isopropyl ketone (IIIb) (50 mg.) in benzene (3 c.c.) was added to one of potassium ethoxide (from 135 mg. of potassium) in ethanol (2·5 c.c.). The solution was stirred and boiled whilst ethyl vinyl ketone [11] (1 c.c.) in ethanol (5 c.c.) was added slowly during 7 hr. Potassium ethoxide (from 23 mg. of potassium) in ethanol (5·5 c.c.) and benzene (1 c.c.) was added, and the mixture was boiled under reflux overnight. The mixture ($\lambda_{max.}$ 445 mμ) was cooled and poured into dilute hydrochloric acid. Isolation of the product as in the previous experiment gave dehydroechinenone (25 mg.), m. p. 170—172° undepressed on admixture with the preceding specimen.

2,6,10,15,19,23-*Hexamethyltetracosa*-4,6,8,10,14,16,18,20-*octaen*-12-*yne*-3,22-*dione* (IVb).—A mixture of 8,8′-dehydrocrocetindial (350 mg.), 3-methylbutan-2-one (6 c.c.), and 5% ethanolic potassium hydroxide (8 c.c.) was shaken occasionally and kept at 20° for 18 hr. The product (330 mg.) which had crystallised had m. p. 192—195°. Recrystallisation from benzene–methanol gave the *diketone* (310 mg.) as deep-orange plates, m. p. 193·5—195° (Kofler block) (Found: C, 83·2; H, 8·75. $C_{30}H_{38}O_2$ requires C, 83·65; H, 8·9%).

15,15′-*Dehydrocanthaxanthin* (IVc).—A solution of the preceding diketone (43 mg.) in benzene (3 c.c.) was added to one of potassium ethoxide (from 154 mg. of potassium), in ethanol (3 c.c.). 1-Diethylaminopentan-3-one methiodide (1·2 g.) in alcohol (6·0 c.c.) was added, and the mixture ($\lambda_{max.}$ 454 and 485 mμ) was stirred and boiled under reflux for 2½ hr. Potassium ethoxide (from 100 mg. of potassium) in ethanol (6 c.c.) was added, and the mixture was boiled for another 18 hr. The mixture ($\lambda_{max.}$ 440 mμ) was cooled and poured into dilute hydrochloric acid. Extraction of the product with benzene–light petroleum (b. p. 60—80°), chromatography from benzene–light petroleum (b. p. 60—80°) on alumina, collection of the main band, evaporation, and crystallisation of the residue from benzene–light petroleum (b. p. 60—80°) gave pale-red needles (23 mg.), m. p. 187—190°. Recrystallisation from chloroform–light petroleum (b. p. 60—80°) gave dehydrocanthaxanthin, m. p. 192—193° (Kofler block) (Found: C, 85·7; H, 8·7. Calc. for $C_{40}H_{50}O_2$: C, 85·35; H, 8·95%). It was identical with the product described by Isler *et al.*[1] (mixed m. p. and chromatogram, comparison of visible, infrared, and nuclear magnetic resonance spectra), who report m. p. 187—188° (uncorr.), $\lambda_{max.}$ (light petroleum) 438 mμ.

15,15′-cis-*Echinenone*.—A solution of 15,15′-dehydroechinenone (27·5 mg.) in ethyl acetate (4 c.c.) was shaken with Lindlar's [12] catalyst (32 mg.) in the dark in an atmosphere of hydrogen until 1·15 mol. of the latter had been absorbed (30 min.). Removal of catalyst and solvent in the dark at 20°, and crystallisation of the residue from light petroleum (b. p. 60—80°) gave 15,15′-*cis*-echinenone (24 mg.), m. p. 156—158° (Kofler block); $\lambda_{max.}$ 454 and 349 mμ, ε = 84,000 and 43,000, respectively, [light petroleum (b. p. 60—80°)].

A solution of the *cis*-isomer (7 mg.) in light petroleum (b. p. 60—80°) containing a trace of iodine was kept in sunlight for 2½ hr. and then evaporated. Crystallisation of the residue from benzene–methanol gave a solid (4·5 mg.), m. p. 170—176°. Recrystallisation from the same

[11] Woodward, Sondheimer, Taub, Heusler, and Mclamore, *J. Amer. Chem. Soc.*, 1952, **74**, 4223.
[12] Lindlar, *Helv. Chim. Acta*, 1952, **35**, 446.

solvent gave " all-*trans* "-echinenone, m. p. and mixed m. p. 176—178°; $\lambda_{max.}$ 456 mμ, ε = 118,000 [light petroleum (b. p. 60—80°)].

Analyses were carried out in the microanalytical (Miss J. Cuckney) laboratory of this Department, and the infrared (Mr. R. L. Erskine), and some of the ultraviolet and visible (Mrs. A. I. Boston) light-absorption measurements in the spectrographic laboratory. The authors thank Messrs Hoffmann-La Roche and Co. Ltd. for generous gifts of chemicals. One of them (M. A.) is indebted to the Pakistan Government for a research grant.

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815. *The Configuration of Noradrenaline.*

By P. Pratesi, A. La Manna, A. Campiglio, and V. Ghislandi.

The stereochemical configuration of noradrenaline has been correlated by chemical means with that of the mandelic acid, through 3-hydroxy-4-methoxymandelic acid. The configuration of D(−)-mandelic acid is found for natural lævorotatory noradrenaline. Thereby the steric correspondence between natural noradrenaline and adrenaline has been definitively established. Deductions are possible also regarding the configuration of the β-carbon atom in the 3,4-dihydroxyphenylserines.

Knowledge of the optical configuration of noradrenaline is an important element in interpreting the biochemical behaviour and the biological properties of this catecholamine. Moreover it makes it possible to establish the configurational relations between this base and other substances which are in biogenetic relationship with noradrenaline, such as adrenaline and 3,4-dihydroxyphenylserine.

Attempts to solve the problem of the configuration of noradrenaline have been made on the basis of biochemical data, namely, the decarboxylation of 3,4-dihydroxyphenylserine by means of L-amino-acid decarboxylase.[1,2] These attempts are based on the assumption that the decarboxylase will only attack the isomer with L-configuration at the α-carbon atom and on knowledge of the configuration of the substrate. But since at present the latter cannot be considered to be unequivocally established,[2] it follows that the configurational assignment for noradrenaline is not definitive.

We here report a purely chemical determination of the configuration of noradrenaline.[3] The method followed is similar to that used by us for determining the configuration of adrenaline.[4] It consists of correlating the configuration of the catecholamine with that of a suitably substituted mandelic acid of known configuration, through transformations which exclude racemization or inversion of configuration at the centre of asymmetry.

3-Hydroxy-4-methoxymandelic acid was taken as the reference substance, its configuration having already been determined.[4] Methyl L(+)-3-hydroxy-4-methoxymandelate (XI) was transformed by means of diazomethane into the oily methyl L(+)-3,4-dimethoxymandelate (XII), which with gaseous ammonia gave the L(+)-amide (XIII). By reduction with lithium aluminium hydride in tetrahydrofuran, the latter gave L(+)-O^3O^4-dimethylnoradrenaline (XIV) whose hydrochloride had m. p. 168—169° and $[\alpha]_D^{18}$ +33·6° (1·1% w/v in 50% EtOH).

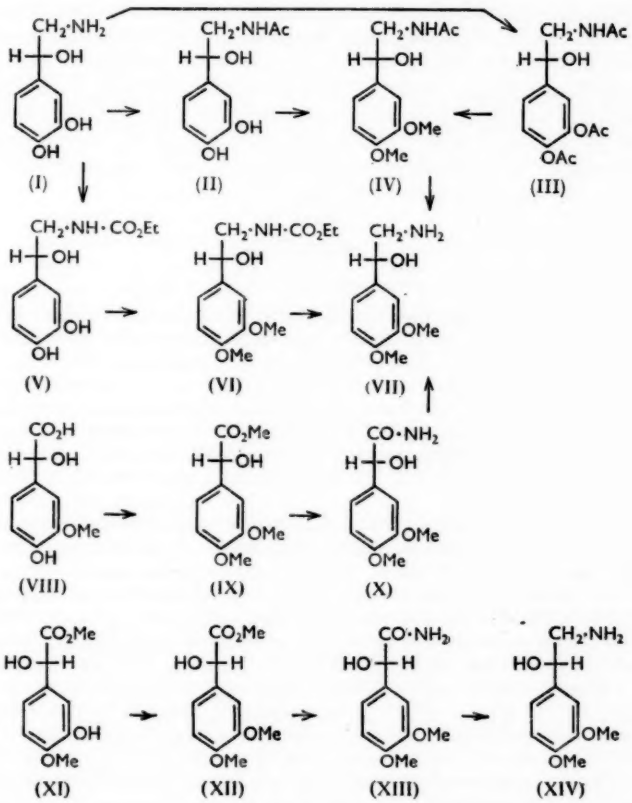
The optical antipode (VII) of the amine (XIV) was obtained from D(−)-4-hydroxy-3-methoxymandelic acid (VIII), prepared by the method of Armstrong, McMillan, and

[1] Blaschko, Holton, and Stanley, *Brit. J. Pharmacol.*, 1948, **3**, 315; Dalgliesh, *J.*, 1953, 3323; Hartman, Pogrund, Drell, and Clark, *J. Amer. Chem. Soc.*, 1955, **77**, 816.
[2] Drell, *ibid.*, p. 5429.
[3] Cf. Pratesi, La Manna, Campiglio, and Ghislandi, Preliminary Communication to the Istituto Lombardo, Accademia di Scienze e Lettere, Milano, Meeting of June 18th, 1959.
[4] Pratesi, La Manna, Campiglio, and Ghislandi, *J.*, 1958, 2069.

Shaw.[5] This acid, treated with diazomethane, gave the oily methyl D(−)-3,4-dimethoxymandelate (IX), from the amide (X) of which D(−)-O^3O^4-dimethylnoradrenaline (VII) was obtained. Its hydrochloride had m. p. 168—169° and $[\alpha]_D^{18}$ −35·7° (1·08% w/v in 50% EtOH).

Thus the configuration of (−)-4-hydroxy-3-methoxymandelic acid, a urinary metabolite of noradrenaline, which had been deduced by Armstrong *et al.*[5] by enzymic resolution of the DL-amide with leucine aminopeptidase, is chemically confirmed.

It still remained to prepare the O^3O^4-dimethyl ether of noradrenaline from the lævorotatory natural base. The latter was acetylated, as described by Bretschneider[6] for



racemic adrenaline, and gave the oily (−)-*N*-acetylnoradrenaline (II), which did not crystallize. By acetylation as described by Welsh[7] for (−)-adrenaline, (−)-noradrenaline gave an oily lævorotatory triacetate (III), which, unlike the racemic compound,[8] could not be obtained crystalline.

Both the crude compounds (II) and (III), treated with dry and wet diazomethane respectively, gave (−)-*N*-acetyl-O^3O^4-dimethylnoradrenaline (IV), which by alkaline hydrolysis, gave (−)-O^3O^4-dimethylnoradrenaline (VII), m. p. 96—97°, $[\alpha]_D^{20}$ −29·7°

[5] Armstrong, McMillan, and Shaw, *Biochem. Biophys. Acta*, 1957, **25**, 422.
[6] Bretschneider, *Monatsh.*, 1948, **78**, 77.
[7] Welsh, *J. Amer. Chem. Soc.*, 1952, **74**, 4967.
[8] Pratesi, La Manna, and Campiglio, *Il Farmaco, Ed. Sci.*, 1959, **14**, 645.

(0·72% w/v in absolute EtOH). Its hydrochloride had m. p. 168—169° and $[\alpha]_D^{18}$ −33·2° (1% w/v in 50% EtOH).

(−)-*N*-Ethoxycarbonylnoradrenaline (V) was also prepared from (−)-noradrenaline. With diazomethane it gave the oily (−)-*N*-ethoxycarbonyl-*O*^{3}*O*^{4}-dimethylnoradrenaline (VI) which, hydrolysed with alkali, gave the amine (VII) again with m. p. 96—97°, $[\alpha]_D^{21}$ −30·3° (0·75% w/v in absolute EtOH); the hydrochloride had m. p. 168—169° and $[\alpha]_D^{20}$ −34·8° (1·08% w/v in 50% EtOH).

As a result of these transformations lævorotatory natural noradrenaline possesses the configuration (I), and thus on the basis of the " sequence rule " [9] it is an (*R*)-form.

The steric correspondence between natural adrenaline [4] and noradrenaline is definitively established by the determination of the configuration of the two catecholamines.

Deductions are possible also regarding the configuration of the 3,4-dihydroxyphenylserines, because the configuration of the β-carbon atom is established. The *threo*-configuration for Dalgliesh and Mann's racemic 3,4-dihydroxyphenylserine, from which Blaschko *et al.*[1] obtained (−)-noradrenaline enzymically, is confirmed. For the same reason the racemate used by Hartman *et al.*,[1] which enzymically gave (+)-noradrenaline, has the *erythro*-configuration. These facts are of interest because of the possibility that 3,4-dihydroxyphenylserine may be a natural precursor of noradrenaline.

Experimental

M. p.s were determined on a Kofler block.

(+)-3,4-*Dimethoxymandelamide* (XIII).—Methyl (+)-3-hydroxy-4-methoxymandelate [4] (XI) (3·5 g.), m. p. 118—119°, $[\alpha]_D^{18}$ +129° (0·55% w/v in EtOH), in anhydrous methanol (50 ml.) was mixed with an ethereal solution of diazomethane (6 g.) and kept for 24 hr. The solution was evaporated *in vacuo*, and the crude methyl (+)-3,4-dimethoxymandelate (XII) taken up in a little dry methanol and saturated at 0° with anhydrous ammonia. After 24 hr. at 0° the mixture was concentrated *in vacuo* and the residue stirred with ethyl acetate. (+)-3,4-*Dimethoxymandelamide* (XIII) so obtained (2·9 g.) crystallized from ethyl acetate; it had m. p. 135—136°, $[\alpha]_D^{18}$ +112·1° (0·45% w/v in $CHCl_3$) (Found: C, 56·8; H, 6·4; N, 6·7. $C_{10}H_{13}O_4N$ requires C, 56·9; H, 6·2; N, 6·6%).

(+)-O^{3}O^4-*Dimethylnoradrenaline* (XIV).—(+)-3,4-Dimethoxymandelamide (1 g.) in hot anhydrous tetrahydrofuran (75 ml.) was added dropwise during 30 min. to a stirred suspension of lithium aluminium hydride (0·8 g.) in tetrahydrofuran (25 ml.) at 70—75°. Stirring was continued for 8 hr. at 70—75°. The next day the mixture was treated with a saturated solution of Rochelle salt, then filtered, and the tetrahydrofuran distilled off *in vacuo*. The residue was dried (P_2O_5) and taken up in a little ethanolic hydrochloric acid. By cooling and rubbing, (+)-O^{3}O^4-*dimethylnoradrenaline hydrochloride* (0·35 g.) was obtained; crystallized from anhydrous 1 : 1 ethanol–ether it had m. p. 168—169°, $[\alpha]_D^{18}$ +33·6° (1·1% w/v in 50% EtOH) (Found: C, 51·6; H, 7·2; N, 6·2. $C_{10}H_{16}O_3NCl$ requires C, 51·4; H, 6·9; N, 6·0%).

(−)-3,4-*Dimethoxymandelamide* (X).—(−)-4-Hydroxy-3-methoxymandelic acid (VIII) (3·2 g.) (obtained as described by Armstrong *et al.*[5]), m. p. 156—157°, $[\alpha]_D^{18}$ −128·9° (0·86% w/v in H_2O), was dissolved in anhydrous methanol (15 ml.) and treated with ethereal diazomethane as described above. By treatment with anhydrous ammonia (−)-3,4-*dimethoxymandelamide* (2·3 g.) was obtained which, crystallized from ethyl acetate, had m. p. 135—136°, $[\alpha]_D^{20}$ −115·4° (0·45 w/v in $CHCl_3$) (Found: C, 56·7; H, 6·2; N, 6·7%).

(−)-N-*Acetyl*-O^{3}O^4-*dimethylnoradrenaline* (IV).—(*a*) (−)-Noradrenaline [10·1 g.; m. p. 215—217°, $[\alpha]_D^{18}$ −36·8° (5% w/v in 0·1N-HCl)] was acetylated as described by Bretschneider [6] for (±)-adrenaline. By concentration of ethyl acetate extract, oily (−)-*N*-acetylnoradrenaline (II) (9·3 g.) was obtained, which did not crystallize even after chromatography in ethanol on alumina and elution with the same solvent. This oily crude (−)-*N*-acetylnoradrenaline (6·0 g.) in anhydrous methanol (100 ml.) was treated in several portions with a large excess of ethereal diazomethane, with cooling and shaking. After 24 hr. the mixture was evaporated *in vacuo*. The oily residue was chromatographed in methanol–ether (1 : 10) on alumina. Elution with the same solvent mixture gave the oily product, which, cooled and stirred with a little ethyl

[9] Cahn, Ingold, and Prelog, *Experientia*, 1956, **12**, 81.

acetate, crystallized. (−)-N-*Acetyl*-O^{3}O^4-*dimethylnoradrenaline* (IV) so obtained (1·4 g.) recrystallized from ethyl acetate: it had m. p. 77—78°, $[\alpha]_D^{19}$ −52·5° (0·95% w/v in $CHCl_3$) (Found: C, 60·1; H, 7·4; N, 5·9. $C_{12}H_{17}O_4N$ requires C, 60·2; H, 7·2; N, 5·8%).

(*b*) The oily crude (−)-*O*^{3}*O*^{4}*N*-triacetylnoradrenaline (III) (3·0 g.) [obtained by direct acetylation of (−)-noradrenaline as described by Welsh [7] for (−)-adrenaline], which did not crystallize even after chromatography, was treated in methanol (35 ml.) with wet ethereal diazomethane, as described above. After 48 hr. the mixture was evaporated *in vacuo* and the oily residue dissolved in methanol–ether (1 : 10) and chromatographed on alumina. By concentration of the eluates, (−)-*N*-acetyl-*O*^{3}*O*^{4}-dimethylnoradrenaline (IV) (1·1 g.) was obtained; it had m. p. and mixed m. p. 77—78°, $[\alpha]_D^{19}$ −51·8° (0·94% w/v in $CHCl_3$) (Found: C, 60·3; H, 7·3; N, 5·9%).

(−)-N-*Ethoxycarbonylnoradrenaline* (V).—(−)-Noradrenaline (9·7 g.) was dissolved, under hydrogen, in 2N-sodium hydroxide (57·6 ml.); to this solution, at 5—10°, with stirring, was added every 10 min. 2N-sodium hydroxide (5 ml.) and ethyl chlorocarbonate in chloroform (5 ml.) (5·5 ml. of ethyl chlorocarbonate and 24·5 ml. chloroform). The mixture was stirred 30 min. and acidified with 4N-hydrochloric acid (57 ml.) and, after saturation with ammonium sulphate, extracted with ethyl acetate (4 × 150 ml.). The dried extract (Na_2SO_4), evaporated under hydrogen, gave an oil (12·0 g.). A sample of this was chromatographed in anhydrous ethanol on alumina. Elution with the same solvent gave (−)-N-*ethoxycarbonylnoradrenaline* (V), m. p. 43—44°, $[\alpha]_D^{19}$ −11·6° (0·7% w/v in anhydrous EtOH) (Found: C, 55·2; H, 6·4; N, 5·9. $C_{11}H_{15}O_5N$ requires C, 54·8; H, 6·3; N, 5·8%).

(−)-N-*Ethoxycarbonyl*-O^{3}O^4-*dimethylnoradrenaline* (VI).—(−)-*N*-Ethoxycarbonylnoradrenaline (3·0 g.) in methanol (25 ml.) was treated with ethereal diazomethane. After 24 hr. the mixture was evaporated *in vacuo*. The oily yellow residue (3·0 g.) was chromatographed in methanol on alumina. Elution with the same solvent and evaporation gave again oily (−)-*N*-ethoxycarbonyl-*O*^{3}*O*^{4}-dimethylnoradrenaline. This was dried and analysed. It had $[\alpha]_D^{18}$ −5·9° (1·51% w/v in anhydrous EtOH) (Found: C, 58·6; H, 7·3; N, 5·4. $C_{13}H_{19}O_5N$ requires C, 58·0; H, 7·1; N, 5·2%).

(−)-O^{3}O^4-*Dimethylnoradrenaline* (VII).—(*a*) (−)-3,4-Dimethoxymandelamide (X) (1·0 g.) in anhydrous tetrahydrofuran (75 ml.) was reduced by lithium aluminium hydride (0·8 g.) as described above for its optical antipode. (−)-O^{3}O^4-*Dimethylnoradrenaline hydrochloride* (0·48 g.) (from ethanol–ether) had m. p. 168—169°, $[\alpha]_D^{18}$ −35·7° (1·08% w/v in 50% EtOH) (Found: C, 51·3; H, 7·0; N, 6·1%).

(*b*) (−)-*N*-Acetyl-*O*^{3}*O*^{4}-dimethylnoradrenaline (IV) (2·1 g.) was dissolved in 2N-sodium hydroxide (15 ml.), and the solution was heated at 110° for 1 hr. After cooling, the alkaline mixture was extracted with ethyl acetate (4 × 150 ml.); the extract, when dried (Na_2SO_4) and evaporated, gave (−)-O^{3}O^4-*dimethylnoradrenaline* (VII) (0·5 g.) which, crystallized from ethyl acetate, had m. p. 96—97°, $[\alpha]_D^{20}$ −29·7° (0·72% w/v in absolute EtOH) (Found: C, 60·5; H, 7·6; N, 7·3. $C_{10}H_{15}O_3N$ requires C, 60·9; H, 7·7; N, 7·1%). From this base, by treatment with ethanolic hydrochloric acid, (−)-*O*^{3}*O*^{4}-dimethylnoradrenaline hydrochloride (from ethanol–ether) was obtained, having m. p. 168—169°, $[\alpha]_D^{18}$ −33·2° (1% w/v in 50% EtOH) (Found: C, 51·4; H, 7·1; N, 6·1%).

(*c*) (−)-*N*-Ethoxycarbonyl-*O*^{3}*O*^{4}-dimethylnoradrenaline (VI) (3·0 g.) was dissolved in 2N-sodium hydroxide (30 ml.) and heated as described above. (−)-*O*^{3}*O*^{4}-Dimethylnoradrenaline (0·61 g.) was obtained by concentration of ethyl acetate extracts; it had m. p. 96—97° (from ethyl acetate) and $[\alpha]_D^{21}$ −30·3° (0·75% w/v in absolute EtOH) (Found: N, 7·1%). Its hydrochloride (from ethanol–ether) had m. p. 168—169°, $[\alpha]_D^{20}$ −34·8° (1·08% w/v in 50% EtOH) (Found: C, 51·2; H, 6·9; N, 6·1%).

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816. *The Oxidation of Diphenylmethylenecyclobutane.*

By S. H. Graham and A. J. S. Williams.

A practicable route for the conversion of cyclobutanecarboxylic acid to cyclobutanone has been devised. Oxidation of diphenylmethylenecyclobutane by electrophilic reagents, such as peracids and chromic acid, involves rearrangement. Rearrangement also accompanies attack by ozone, confirming the electrophilic nature of the process, but oxidation by potassium permanganate or osmium tetroxide proceeds without rearrangement. Addition of hydrogen bromide or of bromine also probably occurs without rearrangement.

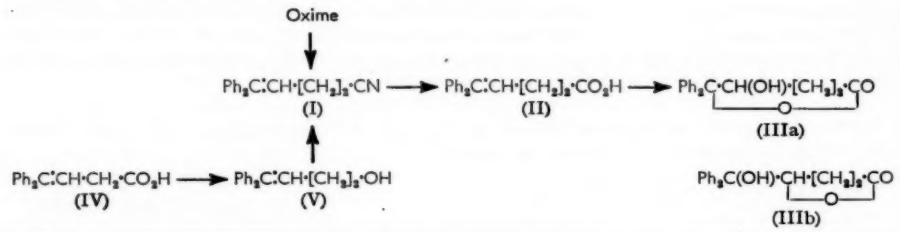
While there are satisfactory methods for the preparation of cyclobutanone, in particular the reaction of keten with diazomethane,[1] these could not be extended to the preparation of alkylcyclobutanones. Degradation of alkylcyclobutanecarboxylic acids seemed to offer a possible route to the substituted ketone.

Whilst methylenecyclobutane can be oxidised to cyclobutanone [2] the oxidation of diphenylmethylenecyclobutane with performic acid, and with other oxidising agents, has been found to proceed differently.

Kishner [3] claims to have oxidised diphenylmethylenecyclobutane to benzophenone by chromic acid. We have found that it is oxidised in good yield to 2,2-diphenylcyclopentanone by chromium trioxide in acetic acid, and that diphenylcyclobutylmethanol is oxidised to the same ketone by chromic acid in aqueous sulphuric acid. The structure of the olefin has therefore been confirmed by converting it by osmium tetroxide into a diol which was then oxidised by lead tetra-acetate to a mixture of benzophenone and cyclobutanone.

Oxidation of the olefin with performic or peracetic acid gave a high yield of 2,2-diphenylcyclopentanone.[4] This part of our work was carried before the report by Easton and Nelson [4] was available to us. Consequently we degraded this ketone to confirm its structure, and report our results here.

The oxime of the ketone was converted by phosphorus pentachloride into an unsaturated nitrile (I) which was hydrolysed to an acid that took up one mol. of hydrogen on catalytic hydrogenation. Attempts to confirm the structure of the acid as 5,5-diphenylpent-4-enoic (II) acid by further oxidation were only partially successful. With aqueous alkaline potassium permanganate it gave benzophenone in good yield, but oxalic acid in place of succinic acid. The use of a limited quantity of permanganate led to some benzophenone, together with a lactone, $C_{17}H_{16}O_3$. The same lactone (IIIa or b) was produced by oxidation with performic acid and subsequent hydrolysis. Oxidation of the acid with chromic acid did, however, yield, in addition to benzophenone, a solid mixture in which succinic acid was detected by paper chromatography.



[1] Kaarsemaker and Coops, *Rec. Trav. chim.*, 1951, 1039.
[2] Roberts and Sauer, *J. Amer. Chem. Soc.*, 1949, **71**, 3925.
[3] Kishner, *J. Russ. Phys. Chem. Soc.*, 1910, **42**, 1228.
[4] Cf. Easton and Nelson, *J. Amer. Chem. Soc.*, 1953, **75**, 640.

The structure of the nitrile was therefore established by synthesis. 4,4-Diphenylbut-3-enoic acid (IV) was prepared from benzophenone and diethyl succinate, and reduced to the alcohol (V) which was converted into the bromide and thence into the nitrile identical with that obtained from the ketoxime.

In contrast with the behaviour of diphenylmethylenecyclobutane, methylenecyclobutane is oxidised by performic acid to a hydroxyformate,[2] and diphenylmethylenecyclohexane [5] is oxidised by peracetic acid to an epoxide.

The diol which we obtained by oxidation of diphenylmethylenecyclobutane with osmium tetroxide was dehydrated to diphenylcyclopentanone by warming it at 40° with formic acid, but it was unaffected by acetic acid at the same temperature.

Oxidation of the olefin with potassium permanganate took a different course. In strongly alkaline conditions [6] it gave the same diol as was obtained from osmium tetroxide and thus provides a satisfactory method of proceeding from cyclobutanecarboxylic acid to cyclobutanone. In the absence of added alkali oxidation, in aqueous acetone or aqueous dioxan, rapidly gave benzophenone and oxalic acid, but with the purely aqueous reagent the olefin was recovered largely unchanged. Control experiments showed that 2,2-diphenylcyclopentanone is stable to permanganate under the same conditions.

Diphenylmethylenecyclobutane reacted with almost exactly one mol. of ozone with the production of benzophenone, diphenylcyclopentanone, and 1,3-dibenzoylpropane. We believe that these products result from reaction with ozone and not from autoxidation by molecular oxygen.[7] Further, diphenylmethylenecyclobutane is unaffected by hydrogen peroxide in the absence of added acid, and so none of the products can have resulted from attack on unchanged olefin by peroxide produced during the hydrolysis of an ozonide. The formation of rearrangement products during the ozonolysis agrees with the view that the initial attack of ozone is electrophilic.[8]

In view of the ready oxidative rearrangement of diphenylmethylenecyclobutane the products obtained by other addition reactions were also investigated. Kishner [3] reported the addition of bromine and of hydrogen bromide and stated that the monobromide was unreactive. The same bromide could be prepared from cyclobutyldiphenylmethanol and hydrobromic acid. We repeated the preparation of the bromide from cyclobutyldiphenylmethanol, and confirm that it does not readily release free bromide ion: for example, 48 hours' boiling with potassium hydroxide in aqueous dioxan produced only traces of bromide ion. This stability is rather unexpected for a diphenylmethyl bromide, but on the other hand our other results agree better, though in rather negative fashion, with an unrearranged structure. We have attempted to synthesise those isomeric bromides which could result from rearrangement, and have been unable to do so. Attempts to prepare 2,2-diphenylcyclopentyl bromide from 2,2-diphenylcyclopentanol produced 1,2-diphenylcyclopentene, and this hydrocarbon gave only tar when treated with hydrogen bromide.

The infrared absorption spectrum of the bromide was of no assistance in resolving this point. Derfer, Pickett, and Boord [9] report that all monoalkylcyclobutanes show a band between 909 and 917 cm.$^{-1}$, although this band is absent from the spectrum of methylenecyclobutane.[10] This criterion ceases to be of value when aryl substituents are present: the spectrum of 1,2-diphenylcyclopentene, for example, has a band at 918 cm.$^{-1}$. The bromide does show a weak absorption at this point but no significance can be attached to it.

Dehydration of 2,2-diphenylcyclopentanol under the conditions used for cyclobutyldiphenylmethanol also gives 1,2-diphenylcyclopentene, whose structure has been proved

[5] Lyle, Martin, and Fielding, *ibid.*, 1953, **75**, 4089.
[6] Lapworth and Mottram, *J.*, 1925, **127**, 1628.
[7] Cf. Traubs and Schollner, *Chem. Ber.*, 1958, **91**, 2282.
[8] Wibaut *et al.*, *Rec. Trav. chim.*, 1951, **70**, 1005; 1952, **71**, 761.
[9] Derfer, Pickett, and Boord, *J. Amer. Chem. Soc.*, 1949, **71**, 2482.
[10] Marrison, *J.*, 1951, 1614.

by ozonolysis in excellent yield, to 1,3-dibenzoylpropane, and by hydrogenation to the known 1,2-diphenylcyclopentane.[11]

The addition of bromine to diphenylmethylenecyclobutane was also investigated. In carbon disulphide solution this rapidly gave a nicely crystalline product which, however, was unstable. Our material melted, with decomposition, between 80° and 84°; Kishner [3] reported a value of 91°.

With sodium iodide in dry acetone the dibromide gave back a good yield (79%) of diphenylmethylenecyclobutane. As this reaction involves the removal of both bromine atoms in a concerted process [12,13] it is unlikely to be accompanied by rearrangement and may be taken as establishing the structure of the dibromide. In this case, too, we were unable to secure a sample of the isomeric dibromide, 1,2-dibromo-1,2-diphenylcyclopentane. 1,2-Diphenylcyclopentene reacted with bromine in carbon disulphide, but hydrogen bromide was evolved in the cold: only tar resulted.

Experimental

Cyclobutyldiphenylmethanol.—To the cooled Grignard reagent prepared from bromobenzene (425 g.), magnesium (65 g.), and ether (1 l.) was added methyl cyclobutanecarboxylate [14,15] (131 g.) in ether (400 ml.). The reaction was completed by refluxing for 30 min. The product was decomposed with saturated ammonium chloride, and the ether layer washed once with water and dried (Na_2SO_4). After removal of volatile material at 100°/15 mm., the residue solidified and weighed 242 g. (88%). This material was suitable for dehydration to the olefin, but distilled without decomposition at 128°/0·1—0·2 mm. and, recrystallised from light petroleum, had m. p. 54°. Kishner [3] gives b. p. 198°/13 mm., m. p. 54—54·5°.

Diphenylmethylenecyclobutane.—(i) *By pyrolysis of O-cyclobutyldiphenylmethyl S-methyl xanthate.* The alcohol (5 g.) was stirred for 30 min. with ether (12 ml.), carbon tetrachloride (1 ml.), and powdered sodium hydroxide (0·8 g.). After addition of carbon disulphide (1·2 ml.) the mixture was refluxed for 3 hr. Methyl iodide (1·4 ml.) was added and refluxing was continued for 6 hr. Water (5 ml.) was added to dissolve solids, the ether layer was washed and dried (Na_2SO_4), and the solvent removed at reduced pressure. The residue was heated over a flame for 20 min. The product solidified on trituration with methanol. It recrystallised from methanol as plates, m. p. 56—56·5°. Kishner [3] gives m. p. 58°. A portion liquified when mixed with the alcohol.

(ii) *By catalytic dehydration of the alcohol with iodine.* The alcohol (5 g.) was refluxed with iodine (0·1 g.) in benzene (20 ml.) for 12 hr. After being washed with sodium thiosulphate the product was distilled (b. p. 144°/2 mm.). The brown distillate solidified and was treated with charcoal in light petroleum. The pale brown plates (2·75 g.) melted at 57—58°, not depressed on admixture with the product obtained in (i) above.

(iii) *By dehydration of the alcohol with oxalic acid.* The alcohol (30 g.) was heated with oxalic acid dihydrate (120 g.) at 160° for 4 hr. The molten product was allowed to cool with stirring, and then extracted with ether (3 × 100 ml.), the ethereal extract being washed with dilute aqueous sodium hydroxide and water and dried. The distillate (25 g.) boiled at 110—112°/0·2—0·25 mm. and solidified; it was identical with the product obtained in (i) above.

Oxidation of Diphenylmethylenecyclobutane.—(i) *With performic acid.* To the olefin (2·2 g.) in 90% formic acid (6 ml.) was added, with stirring, hydrogen peroxide (1·4 ml.; 100-vol.), the temperature being kept at 40° for 6 hr. The mixture was left to crystallise, giving 2·16 g. of 2,2-diphenylcyclopentanone, m. p. 88—89° (from light petroleum) (Found: C, 86·0; H, 6·8. Calc. for $C_{17}H_{16}O$: C 86·4; H, 6·8%). The infrared spectrum showed a strong carbonyl absorption band at 1739 $cm.^{-1}$, characteristic of cyclopentanones. Easton and Nelson [4] report m. p. 87·5—89·5°. The 2,4-dinitrophenylhydrazone formed yellow-orange plates (from acetic acid or chloroform–light petroleum), m. p. 180—181°; Easton and Nelson [4] report m. p. 182—182·5°.

[11] von Liebig, *Annalen*, 1914, **405**, 207.
[12] Young, Pressman, and Coryell, *J. Amer. Chem. Soc.*, 1939, **61**, 1640.
[13] Winstein, Pressman, and Young, *ibid.*, p. 1645.
[14] Cason and Allen, *J. Org. Chem.*, 1949, **14**, 1036.
[15] Vogel and Jeffery, *J.*, 1948, 1806.

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(ii) *With peracetic acid and sulphuric acid.* To the olefin (5·4 g.) in acetic acid (21·2 ml.) containing concentrated sulphuric acid (3 ml.) hydrogen peroxide (30 ml.; 100-vol.) was added, dropwise and with stirring, at 40°: the reaction was exothermic. The product (4·9 g.) crystallised out after 1 hr. and was identical with the product obtained in (i) above.

(iii) *With peracetic acid.* A solution of the olefin (0·55 g.) in acetic acid (7 ml.) was heated at 50—55° for 5 hr. with a slight excess of hydrogen peroxide. After removal of the solvent *in vacuo* the residue recrystallised from methanol and then from light petroleum; it melted at 87° alone or mixed with diphenylcyclopentanone.

(iv) *With monoperphthalic acid.* The olefin (1·1 g.) was treated in ether with a slight excess (2·5%) of ethereal monoperphthalic acid. The solution was kept at 0° for 3 days. Phthalic acid was then filtered off and washed with dry chloroform. The combined ether and chloroform filtrate was evaporated *in vacuo*, and the residue extracted three times with hot light petroleum (b. p. 60—80°) and filtered off. The residue, phthalic acid, weighed 0·78 g. (theor. 0·88 g.). Evaporation of the light petroleum gave an oil which did not solidify in 4 days at 0°. Distillation (bath 160°/0·1 mm.) gave diphenylcyclopentanone, m. p. 86—88°, after two crystallisations from light petroleum.

(v) *With chromium trioxide in acetic acid.* To a solution of the olefin (0·5 g.) in acetic acid (5 ml.) at 35° chromium trioxide (0·3 g.), dissolved in acetic acid (0·5 ml.), was added. The reaction was exothermic and the vessel was cooled in running water. The solution was heated at 40° for 30 min.; a test portion then rapidly crystallised when stirred into water. The product was isolated by ether-extraction, washing, and drying. Evaporation of ether gave 2,2-diphenylcyclopentanone (150 mg.). The mother-liquors did not contain benzophenone.

(vi) *With ozone.* Through a solution of the olefin (5·5 g., 0·025 mol.) in dry ethyl acetate (100 ml.) at −10° ozone was passed at the rate of 0·007 mol./hr. for 3·6 hr. During this time the iodine liberated in the potassium iodide bubbler by the exit gases was equivalent to 1·5 ml. of 0·5N-sodium thiosulphate. Ozonolysis was continued for a further 15 min. during which iodine equivalent to 2·4 ml. of 0·5N-sodium thiosulphate was liberated. The solvent was removed *in vacuo* and the residual oil refluxed with water (50 ml.) for 15 min. About 15 ml. of water were distilled off but gave only a faint turbidity when treated with 2,4-dinitrophenylhydrazine in 2N-hydrochloric acid. The residual mixture was extracted with ether (25 ml.), and the ethereal layer was washed with water (20 ml.). This aqueous layer also failed to give a positive carbonyl reaction. The ethereal layer was dried (Na_2SO_4). After removal of ether, distillation of the residue gave a fraction (1·65 g.), b. p. 160°/15 mm., which solidified on being seeded with benzophenone and gave a 2,4-dinitrophenylhydrazone (92% yield), m. p. 235—236° (from acetic acid) alone or mixed with benzophenone 2,4-dinitrophenylhydrazone. The residue was then distilled (bath 140°/0·1 mm.), giving 1·35 g. of crystalline material (A) and a residue (B) which also crystallised. After redistillation followed by recrystallisation from light petroleum and then from methanol, material (A) melted at 87° alone or mixed with 2,2-diphenylcyclopentanone. After two recrystallisations from methanol, material (B) melted at 65° alone or mixed with 1,3-dibenzoylpropane.[16]

Repetition of the experiment on the same quantity of olefin dissolved in glacial acetic acid (25 ml.) containing boron trifluoride–ether complex (3 ml.) gave benzophenone (2·1 g.), 2,2-diphenylcyclopentanone (1·32 g.), and 1,3-dibenzoylpropane (0·25 g.).

(vii) *With osmium tetroxide.* To the olefin (0·88 g.) and osmium tetroxide (1 g.) in dry, distilled, " AnalaR " benzene (8 ml.) was added dry, distilled " AnalaR " pyridine (0·63 g.). An exothermic reaction took place and the mixture was kept at room temperature for 48 hr. Black crystals (1·72 g.) were collected and then stirred with methylene chloride (25 ml.), water (100 ml.), potassium hydroxide (1 g.), and mannitol (10 g.) for 3 hr. The aqueous extract was pink. Crystals (0·7 g.) obtained from the methylene chloride were treated in boiling benzene with charcoal (50 mg.). Dilution of the filtrate with light petroleum gave needles, m. p. 144·5—145·5°, of 1-(*α-hydroxy-αα-diphenylmethyl*)*cyclobutanol* (Found: C, 80·1; H, 7·1. $C_{17}H_{18}O_2$ requires C, 80·3; H, 7·1%).

This diol was dehydrated to 2,2-diphenylcyclopentanone by 90% formic acid at 40° in 6 hr. but was unchanged in glacial or 90% acetic acid at 55° for 6 hr.

(viii) *With potassium permanganate in the absence of added alkali.* Dioxan was purified by refluxing it with sodium for 6 hr., then distilling it, refluxing it with potassium permanganate and sodium hydroxide for 4 hr., and distilling it from this mixture.

[16] Milone and Venturatto, *Gazzetta*, 1936, **66**, 808.

To the olefin (5·6 g.) in this dioxan (25 ml.) and water (6 ml.) potassium permanganate (8 g.) was added in portions. An exothermic reaction took place. Manganese dioxide was filtered off and washed with water. The filtrate was diluted with water and extracted twice with ether. White crystals were extracted from the manganese dioxide with ether. The combined ethereal solution was washed with a little water and dried (Na_2SO_4). Removal of ether gave an oil (4·86 g.) which partly solidified. Distillation gave no clearly defined fractions. A forerun (2·70 g.) boiling below 116°/0·4 mm. was collected. Further distillation gave unchanged olefin (2·16 g.), b. p. 118°/0·4 mm.

The forerun failed to solidify after being kept in the refrigerator for 3 days, but with 2,4-dinitrophenylhydrazine hydrochloride gave benzophenone 2,4-dinitrophenylhydrazone.

The combined aqueous solutions (*ca.* 130 ml.) were filtered to remove traces of manganese dioxide, neutralised with hydrochloric acid, and distilled. Only a turbidity was obtained from this distillate and 2,4-dinitrophenylhydrazine in 2N-hydrochloric acid. The residual aqueous solution from the distillation was passed through a column of Zeocarb 225; evaporation then gave oxalic acid dihydrate, m. p. and mixed m. p. 97—99° (from water).

The dioxan could be replaced by acetone (purified by Conant's method [17]). Unchanged olefin and benzophenone dinitrophenylhydrazone were again isolated but no oxalic acid.

The olefin failed to react with aqueous potassium permanganate at room temperature.

(ix) *With potassium permanganate in the presence of added alkali.* To the olefin (2·2 g.) in purified dioxan (60 ml.) potassium permanganate (3·4 g.) and sodium hydroxide (2·4 g.) in water (100 ml.) were added portionwise with stirring. The mixture did not react at 15° but rapidly deposited manganese dioxide at 40°. The reaction was exothermic and was complete within 20 min. The mixture was filtered and the filtrate extracted with ether (2 × 100 ml.); the manganese dioxide was also stirred with ether. The combined ethereal extracts were washed with water (20 ml.) and dried (Na_2SO_4). Removal of solvents gave 1-(α-hydroxy-αα-diphenylmethyl)cyclobutan-1-ol (1·6 g., 62·6%), m. p. 144·5—145·5° (from benzene–light petroleum), undepressed on admixture with the diol obtained in (vii) above.

Attempted Oxidation of 2,2-Diphenylcyclopentanon with Potassium Permanganate.—The ketone (1 g.) dioxan (purified as above; 5 ml.), water (1 ml.), and potassium permanganate (0·75 g.) were warmed at 50—60° for 15 min. Only the ketone (0·87 g.) was recovered.

Oxidation of 1-(α-Hydroxy-αα-diphenylmethyl)cyclobutan-1-ol with Lead Tetra-acetate.—The diol (350 mg.) in dry methylene chloride (4 ml.) was oxidised with recrystallised lead tetra-acetate (670 mg.) contained in a sintered-glass thimble above the solution. When extraction of the reagent was complete, refluxing was continued for 1 hr. and the mixture then left overnight, boiled with ethanol (30 ml.) and 2,4-dinitrophenylhydrazine (500 mg., 92%), treated with concentrated hydrochloric acid (1 ml.), refluxed for 1 hr., and cooled in ice (7 hr.). The resulting solids were collected and dissolved in chloroform, washed with water, and dried (Na_2SO_4). Evaporation gave 680 mg. (88%) of mixed dinitrophenylhydrazones.

The mixture of dinitrophenylhydrazones (240 mg.), dissolved in chloroform, was separated by chromatography on bentonite–kieselguhr (20 g.).[18] The first component, eluted with chloroform, was benzophenone 2,4-dinitrophenylhydrazone (125 mg.), m. p. and mixed m. p. 237—238°. The second, eluted with chloroform–ethanol (19 : 1), was cyclobutanone 2,4-dinitrophenylhydrazone (90 mg.), m. p. and mixed m. p. 145° after softening at 143° (Roberts *et al.*[2] give m. p. 146—146·5°). Preliminary experiments on the separation of synthetic mixtures of cyclobutanone dinitrophenylhydrazone and dinitrophenylhydrazine showed that the former is best eluted with chloroform–ethanol (19 : 1): use of chloroform–ethanol (7 : 3) results in the elution of the reagent ahead of the derivative.

Oxidation of Cyclobutyldiphenylmethanol with Chromic Acid.—The alcohol (1 g.) reacted very vigorously with chromium trioxide (0·7 g.), water (1·5 ml.), and concentrated sulphuric acid (0·75 ml.) to give, after extraction with ether and the usual working up, 2,2-diphenylcyclopentanone (70%).

2,2-Diphenylcyclopentanone Oxime.—To the ketone (8·2 g.) in ethanol (120 ml.) sodium hydroxide (6 g.) and hydroxylamine hydrochloride (5 g.) were added in concentrated aqueous solution. After 6 hours' refluxing alcohol (70 ml.) was distilled off and the cooled residue stirred into dilute hydrochloric acid. Recrystallisation of the resulting solid from methanol

[17] Conant, *J. Amer. Chem. Soc.*, 1924, **46**, 245.
[18] Cf. Elvidge and Whalley, *Chem. and Ind.*, 1955, 589.

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(*ca.* 40 ml./g.) gave the *oxime* (7 g., 80%) as needles, m. p. 172° (Found: C, 81·4; H, 6·6; N, 6·0. $C_{17}H_{17}ON$ requires C, 81·2; H, 6·8; N, 5·6%).

The oxime (8 g.) in dry ether (250 ml.) was treated with phosphorus pentachloride (11 g.) and kept overnight at room temperature. After removal of ether the residue was boiled with water, then cooled, and the product collected (6·3 g., 85%). Recrystallisation from methanol gave elongated plates, m. p. 68°, not depressed on admixture with 4-cyano-1,1-diphenylbut-1-ene (see below).

5,5-Diphenylpent-4-enoic Acid.—The nitrile (5 g.) was refluxed for 10 hr. with potassium hydroxide (10 g.) in ethanol (70 ml.) and water (15 ml.). Ethanol was distilled off, water (100 ml.) was added, and the mixture extracted with ether. Acidification of the aqueous layer gave *5,5-diphenylpent-4-enoic acid* (4·5 g. crude), m. p. 82—83° (plates, from light petroleum) (Found: C, 80·8; H, 6·1. $C_{17}H_{16}O_2$ requires C, 80·9; H, 6·4%).

Oxidation of 5,5-Diphenylpent-4-enoic Acid with Alkaline Potassium Permanganate.—(i) To the acid (2·5 g.) in aqueous potassium hydroxide (0·8 g. in 20 ml.) potassium permanganate (14 g.) in water (200 ml.) was added dropwise with stirring at 40°. Manganese dioxide was filtered off and then stirred with ether. The aqueous filtrate was also extracted with ether. The combined ether extracts contained 1·1 g. (60%) of benzophenone, m. p. and mixed m. p. 45—47° (from light petroleum) (2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 238°).

A little hydrogen peroxide was added to the aqueous layer to remove potassium permanganate, and the solution was heated on the steam-bath to decompose hydrogen peroxide and then passed through a column of Zeocarb 225. Evaporation of the eluate at 45°/15 mm. gave 1·3 g. of oxalic acid dihydrate, m. p. and mixed m. p. 100° (from aqueous methanol).

(ii) The acid (1 g.) was treated with water (10 ml.) and potassium hydroxide (0·32 g.). To this solution was added potassium permanganate (1·68 g.) in water (60 ml.) at 40°. Manganese dioxide was precipitated at once and the colour of potassium permanganate was discharged after warming for 5 min. The mixture was worked up as above. The solvent layer contained benzophenone isolated as its 2,4-dinitrophenylhydrazone (250 mg.), m. p. 237°. On passing the aqueous layer through Zeocarb 225 the eluate was found to contain *4,5-dihydroxy-5,5-diphenylvaleric γ- or δ-lactone* which, recrystallised from methanol, then benzene–light petroleum, had m. p. 174° (Found: C, 76·1; H, 5·8. $C_{17}H_{16}O_3$ requires 76·1; H, 6·0%). A further quantity of lactone was obtained by stirring the extruded resin with ether.

γδ-Dihydroxy-δδ-diphenylvaleronitrile.—4-Cyano-1,1-diphenylbut-1-ene (1·17 g.) was stirred at 40° for 2 hr. with 90% formic acid (5 ml.) containing a slight excess of hydrogen peroxide (0·6 ml.; 100-vol.). The resulting crystals were recrystallised from methanol and then from benzene, giving fine needles of *4,5-dihydroxy-5,5-diphenylvaleronitrile*, m. p. 154—155° (Found: C, 76·3; H, 6·5; N, 4·9. $C_{17}H_{17}O_2N$ requires C, 76·4; H, 6·4; N, 5·2%).

This nitrile (400 mg.) was refluxed with potassium hydroxide (1 g.) in ethanol (10 ml.) and water (1·5 ml.) until no more ammonia was evolved (4 hr.). Pouring the products into water (30 ml.) and acidifying them with concentrated hydrochloric acid gave the above lactone, m. p. 173°, sparingly soluble in methanol.

Oxidation of 5,5-Diphenylpent-4-enoic Acid with Chromic Acid.—The unsaturated acid (170 mg.) was heated at 40° with chromium trioxide (150 mg.) in acetic acid (3 ml.). The mixture was diluted with water and extracted with ether. The usual working up of the ether layer gave an oil which gave benzophenone 2,4-dinitrophenylhydrazone. The aqueous layer was warmed with ethanol in order to reduce chromic acid, then passed through Zeocarb 225. The colourless eluate was evaporated under reduced pressure leaving a whitish solid which was shown to contain succinic acid by paper chromatography in ammonia–ethanol. An attempt to isolate succinic anhydride by vacuum-sublimation was unsuccessful.

4,4-Diphenylbut-3-en-1-ol.—4,4-Diphenylbut-3-enoic acid [19] (9·4 g.) was esterified by ethereal diazomethane (yield, 8·85 g.; b. p. 128°/0·2 mm.). The ester (8 g.) in ether (50 ml.) was added dropwise, with stirring, to lithium aluminium hydride (1·2 g.) suspended in ether (150 ml.). After 2 hours' refluxing and storage overnight a grey sticky complex had separated. Ethyl acetate (6 ml.) was added, then crushed ice, followed by 2N-sulphuric acid (80 ml.). The ethereal layer was washed with dilute sodium carbonate and water, and dried (Na_2SO_4). Distillation gave the alcohol (4·29 g.), b. p. 138—140°/0·18—0·20 mm. [*3,5-dinitrobenzoate*, m. p. 129—130° (from benzene–light petroleum, then aqueous dioxan, then benzene–light petroleum) (Found: C, 66·0; H, 4·3; N, 6·7. $C_{23}H_{16}O_6N_2$ requires C, 66·0; H, 4·3; N, 6·7%)].

[19] Johnson, Peterson, and Schneider, *J. Amer. Chem. Soc.*, 1947, **69**, 74.

4-Cyano-1,1-diphenylbut-1-ene.—Bromine (1·43 g.) was added to triphenyl phosphite (2·77 g.) at 0°. The mixture was kept for 30 min., then stirred with 4,4-diphenylbut-3-en-1-ol (2 g.) for a further 30 min. After 30 minutes' heating at 100° the product was dissolved in chloroform, washed with dilute sodium hydroxide and water, and dried (Na_2SO_4). The residue remaining after removal of solvent weighed 3·85 g. Distillation gave 4-bromo-1,1-diphenylbut-1-ene (1·26 g.), b. p. 140—148°/0·35 mm., and triphenyl phosphate (1·75 g.), b. p. 160—180°/0·3 mm., m. p. 49° (lit., b. p. 245°/11 mm., m. p. 49°).

This bromide (1·26 g.), ethanol (8 ml.), potassium cyanide (0·33 g.), and water (1 ml.) were refluxed for 24 hr. The solvent was removed *in vacuo*, and the residue was dissolved in ether, washed, dried (Na_2SO_4), and evaporated. Then recrystallisation from light petroleum (charcoal) gave 4-cyano-1,1-diphenylbut-1-ene (0·26 g.), m. p. 65—66° (Found: C, 87·4; H,6·5; N, 5·8. $C_{17}H_{15}N$ requires C, 87·5; H, 6·5; N, 6·0%).

Reaction between Cyclobutyldiphenylmethanol and Hydrogen Bromide.—The alcohol (2 g.) was kept overnight at room temperature with a 22% w/v solution (20 ml.) of hydrogen bromide in acetic acid, and the resulting dark red solution was poured into water. The bromide, recrystallised from methanol, had m. p. 94—95° (1·75 g., 70%); Kishner [3] gives m. p. 94—95°. If the mixture was heated a tar was obtained.

2,2-Diphenylcyclopentanol.—2,2-Diphenylcyclopentanone (10·5 g.) in dry ether (200 ml.) was added, with stirring, to lithium aluminium hydride (6 g.) suspended in ether (150 ml.). After 6 hours' refluxing, ethyl acetate (25 ml.) was added, then ice and 2N-sulphuric acid (300 ml.). The ethereal layer was separated, the aqueous layer was extracted once with ether (100 ml.), and the combined ethereal solutions were washed with 2N-sodium hydroxide and water and dried (Na_2SO_4). Distillation gave *2,2-diphenylcyclopentanol* (8·7 g., 82%), b. p. 132°/0·2 mm., m. p. 51—52° [needles, from light petroleum (b. p. 40—60°)] (Found: C, 85·5; H, 7·6. $C_{17}H_{18}O$ requires C, 85·7; H, 7·6%) [*3,5-dinitrobenzoate*, m. p. 122° (from benzene–light petroleum) (Found: C, 66·8; H, 4·9; N, 6·6. $C_{24}H_{20}O_6N_2$ requires C, 66·7; H, 4·7; N, 6·5%)].

Reaction between 2,2-Diphenylcyclopentanol and Triphenyl Phosphite Dibromide.—Triphenyl phosphite dibromide [20] was prepared from triphenyl phosphite (7·75 g.) and bromine (4 g.) at 0°. The cyclopentanol (6 g.) was added and the mixture heated at 60° for 45 min. Within a few seconds the colour changed to greenish-blue and fumes were evolved. The mixture was cooled, dissolved in chloroform, washed with 2N-sodium hydroxide and water, and dried (Na_2SO_4). Distillation gave *1,2-diphenylcyclopentene* (4·28 g., 77·4%), b. p. 114°/0·1 mm., m. p. 62·5—63° (needles, from methanol) (Found: C, 92·7; H, 7·1. $C_{17}H_{16}$ requires C, 92·7; H, 7·3%); Weidlich and Meyer-Delius [21] describe it as a liquid. The residue from the distillation was triphenyl phosphate.

After a reaction at room temperature overnight, the product failed to crystallise on trituration with solvents and storage at 0°.

Dehydration of 2,2-Diphenylcyclopentanol.—The alcohol (0·75 g.) was dehydrated by oxalic acid dihydrate (3 g.) at 150—160° for 4 hr. to 1,2-diphenylcyclopentene. The same compound was produced by prolonged refluxing of the alcohol with hydrogen bromide in acetic acid (22% w/v).

Ozonolysis of 1,2-Diphenylcyclopentene.—The cycloalkene (1 g.) in dry ethyl acetate (50 ml.) was treated with ozone (4×10^{-3} mole/hr.) at 0°. After the calculated time the contents of the trap bottle containing potassium iodide were titrated, and ozonisation continued for a further 15 min., during which iodine was rapidly liberated by the exit gases. The solvent was then removed *in vacuo* and the residue treated with peracetic acid.[22] This gave 1,3-dibenzoylpropane (1 g. 87%), m. p. and mixed m. p. 65—66°.

Hydrogenation of 1,2-Diphenylcyclopentene.—The cycloalkene (220 mg.) was hydrogenated over Adams catalyst (50 mg.) in ethyl acetate (15 ml.) containing ethanol (1 ml.). Uptake of hydrogen was 24·8 ml. at 21°/758 mm. (one double bond, 24·8 ml.). Removal of solvent and recrystallisation from methanol gave 1,2-diphenylcyclopentane, m. p. 45—46° (lit.,[11] 46°).

1-Bromo-1-(α-bromo-αα-diphenylmethyl)cyclobutane.—Diphenylmethylenecyclobutane (2 g.) in carbon disulphide was treated portionwise with a slight excess of bromine in carbon disulphide (5% v/v) at room temperature. Evaporation, followed by recrystallisation from light

[20] Cf. Landauer and Rydon, *J.*, 1954, 2281.
[21] Weidlich and Meyer-Delius, *Ber.*, 1941, **74**, 1195.
[22] Cf. Henne and Hill, *J. Amer. Chem. Soc.*, 1943, **65**, 752.

petroleum, gave a solid (1·7 g.) melting between 70° and 80° to a green liquid; some hydrogen bromide was evolved during the recrystallisation. On further crystallisation from light petroleum, hydrogen bromide was again evolved, the melting range being 80—84° (decomp.): Kishner [3] reports m. p. 91—92°.

This material (1·7 g.) was refluxed in dry acetone (10 ml.) with sodium iodide (0·7 g.) for 1 hr., then extracted with ether. Extraction with aqueous sodium thiosulphate and then with 2N-sodium hydroxide failed to remove a deep red colour from the ethereal layer. The ethereal solution was washed with water and dried (Na_2SO_4). Evaporation gave black crystals. Distillation (bath 140—150°/0·2 mm.) and one recrystallisation from methanol gave diphenylmethylenecyclobutane (780 mg., 79%), m. p. and mixed m. p. 56—56·5°.

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817. *Infrared Spectra and Structure of Some Simple and Bridged Nitro-complexes of Platinum, Palladium, and Cobalt.*

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The infrared spectra of some dinitro-complexes of platinum(II), palladium(II), and cobalt(III) have been examined. The spectra of the *trans*-isomers have bands (some of which are split) in the regions around 1415 (ν_3), 1330 (ν_1), and 822 cm.$^{-1}$ (ν_2). The *cis*-isomers have somewhat similar spectra with ν_1 shifted to rather lower frequency and the characteristic addition of a band at about 1350 cm.$^{-1}$; also ν_2, which is a single band in the spectra of the *trans*-isomers, is sharply split in the spectra of the *cis*-isomers. Two binuclear complexes having bridging nitro-groups were also examined. Their spectra have bands due to bridging nitro-groups near 1480 and 1200 cm.$^{-1}$. From these we infer that the nitro-group forms bridges through the nitrogen and one oxygen atom as hitherto assumed, *viz.*, M–N(O)–O–M. The spectra of a number of mononitro- and polynitro-complexes are also recorded.

Beattie and Tyrrell [1] examined some nitroammine complexes of tervalent cobalt in the infrared region between 4000 and 700 cm.$^{-1}$ using the potassium bromide disc technique; it was concluded that the geometrical isomers of the dinitrotetramminecobalt(III) complex may be distinguished by examination of the spectra in the 1300 and 850 cm.$^{-1}$ regions. Nakamoto *et al.*[2] have also interpreted the splitting of the cobalt–ammonia stretching frequencies in various nitroammines in a similar manner. It had been suggested earlier [3] that the spectrum of the *cis*-dinitrotetramminecobalt(III) cation, $[Co^{III}(NO_2)_2(NH_3)_4]X$ where X = a singly charged anion, should show more bands than the *trans*-isomer, owing to the lower symmetry. An extra band was observed for the *cis*-isomer in the 1350 cm.$^{-1}$ region.

The present work was undertaken to ascertain whether there were features in the infrared spectra which could be used to distinguish between *cis*- and *trans*-isomers of planar complexes, and if possible to assign absorption bands characteristic of bridging nitro-groups. The variation of NO_2 stretching frequencies with different electronic effects transmitted through the metal atom was also investigated.

Results and Discussion.—The frequencies of the NO_2 absorption bands of the compounds examined are given in Tables 1—4.

[1] Beattie and Tyrrell, *J.*, 1956, 2849.
[2] Nakamoto, Fujita, and Murata, *J. Amer. Chem. Soc.*, 1958, **80**, 4817.
[3] Faust and Quagliano, *J. Amer. Chem. Soc.*, 1954, **76**, 5346.

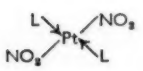
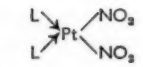
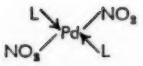
The most recent assignment of the absorption frequencies for the non-linear triatomic NO_2^- group, which belongs to the point group C_{2v}, are given below together with the vibration type.[4] All three fundamental frequencies are active in the infrared region of the spectrum. These vibration types also occur when the NO_2 group is co-ordinated to a metal atom as the local symmetry of the group remains the same.

Type	No.	ν (cm.$^{-1}$)	Assignment
A_1	ν_1	1328 ± 2	Symm. stretch
A_1	ν_2	828·2 ± 0·4	NO_2 bend
B_1	ν_3	1261 ± 3	As. stretch

The above assignment of ν_1 and ν_3 is incorrect because the asymmetric vibration always has the higher of the stretching frequencies. This has been assumed in our assignment of bands in the spectra of the complexes. Table 1 gives the NO_2 frequencies of a series of platinous and palladous nitro-complexes *cis*- and *trans*-$[L_2Pt(NO_2)_2]$ and *trans*-$[L_2Pd(NO_2)_2]$ containing a variety of uncharged ligands (L), examined in chloroform solution. The bending frequencies were obtained from acetone solutions. The ligands include, *e.g.*, amines, di-n-butyl sulphide, tri-n-butylphosphine, and tri-n-butylarsine.

The symmetric stretching modes of $NO_2(\nu_1)$ produce sharp bands in the range 1340—1318 cm.$^{-1}$, whereas the asymmetric stretching modes (ν_3) cause broader absorption bands, often with several shoulders, the principal maxima of which lie in the range 1440—1390 cm.$^{-1}$. The strongest band in the 1400 cm.$^{-1}$ region is considered to be the asymmetric NO_2 stretching band. The *cis*-isomers have, in addition, a third fairly broad band in the region 1355—1337 cm.$^{-1}$. This almost certainly is due to the lower symmetry of the *cis*- than of the *trans*-compounds, and would arise from the out-of-phase symmetric vibration of the two NO_2 groups. An alternative explanation, that it arises from steric interactions of the neighbouring NO_2 groups whereby one of the NO_2 groups is twisted out of the plane of the complex, as has been postulated to account for the splitting of the nitro-group frequencies in *o*-dinitroaryl compounds,[5] is very unlikely. With the greater angle between the nitro-groups in the complexes, their steric interaction will be very small indeed.

TABLE 1. NO_2 *absorption frequencies* (*cm.*$^{-1}$) *of some platinous and palladous complexes.*

	L	pepy *	PBu^n_3	$AsBu^n_3$	Bu^n_2S	Pr^n_2Se	Pr^n_2Te
	as.	1412 b	1394 b	1401 b	1419 b	1423 sh 1409 b	1418 sh 1400 b
	sym.	1337	1328	1328	1333	1331	1326
	bend	822	819	—	820 s 822 w.sh	—	—
	as.		1418 sh 1401 1382 sh		1432 b 1416 sh		
	sym.		1337 b 1323 sh		1347 b 1322		
	bend		817 } 798 }		825 } 818 }		
	as.	1411 b	1412 sh † 1396 b	1400 b	1426 sh † 1413 b	1426 sh 1410 b	1420 sh 1401 b
	sym.	1332	1327	1324	1327	1325	1321

* pepy = 4-n-pentylpyridine; s = strong; w = weak; sh = shoulder; b = broad.
† The splittings were observed by using a grating instrument.

In the 800 cm.$^{-1}$ region, examined in acetone, ν_2 appears as a single sharp band in the range 822—819 cm.$^{-1}$ for the *trans*-isomers, whereas the *cis*-isomers have two sharp and

[4] Weston and Brodasky, *J. Chem. Phys.*, 1957, **27**, 683.
[5] Bellamy, " The Infra-Red Spectra of Complex Molecules," Methuen, London, 1958, p. 301.

quite distinct bands in the ranges 825—817 cm.$^{-1}$ and 818—798 cm.$^{-1}$. The double peak arises because in the *cis*-compound both the in-phase and the out-of-phase vibration are infrared-active. This splitting in the case of the *cis*-isomers and the presence of an additional band in the 1350 cm.$^{-1}$ region are considered to be characteristic of these isomers on the basis of the above compounds and the bisethylenediaminecobalt(III) complexes to be described here.

It is immediately apparent that no simple relation exists between the values of the NO_2 stretching frequencies, within the above defined ranges, and the type of donor atom in the uncharged ligands. In the *trans*-platinous or -palladous complexes the highest values of the asymmetric frequencies occur when di-n-butyl sulphide is the uncharged ligand (L), and the lowest frequencies when tri-n-butylphosphine is the donor group. On the other hand, the highest symmetric NO_2 frequencies occur when L is an amine, and the lowest when L is di-n-propyl telluride.

The factors affecting the NO_2 stretching frequencies in these compounds are obviously complicated, and the frequencies alone do not lend themselves to any obvious interpretation in terms of electronic effects transmitted through the metal atoms from the ligands (L). However, the fact that the frequencies do not follow a sequence parallel to that of the electronegativities of the donor atoms in L implies that something other than the inductive effects of the ligands is transmitted across the metal atoms to the nitro-groups. One such an effect could be caused by d_π-bonding between donor atoms with vacant *d*-orbitals of suitable energy in the ligand L, and the metal atom.

Bisethylenediaminecobalt(III) *complexes.* A series of mononitro-complexes of bisethylenediaminecobalt(III) was first examined, and by comparison with the spectrum of trisethylenediaminecobalt(III) chloride, and other complexes not containing nitro-groups, the frequencies listed in Table 2 were deduced for the nitro-groups. From this series of

TABLE 2. *Nitro-group frequencies (cm.$^{-1}$) of complexes of the type* $[Co(en)_2(NO_2)Y]X$.

trans-*Isomers*					cis-*Isomers*				
Y	X	ν_3	ν_1	ν_2	Y	X	ν_3	ν_1	ν_2
SCN	SCN	1418 s	1318 s	825 s	Cl	NO_3	1404 s	1323, 1312 s	826 s
SCN	Cl	1413 s	1326 s	822 s	SCN	Cl	1416 s	1318 s	819 s
SCN	NO_2	1410 s	1326 s	820 s	SCN	NO_2	1416 s	1323 s	819 s
Cl	SCN	1427 s	1335 s	824 s	Cl	Cl	1401 s	1319 s	825 s

en = ethylenediamine; s = strong.

mononitro-complexes, it is apparent that there is little variation in frequency when the nitro-group is *cis*- or *trans*- to the other anionic ligands present. The frequency ranges observed were: ν_3, 1414 ± 13; ν_1, 1323 ± 12; ν_2, 822 ± 4 cm.$^{-1}$.

TABLE 3. *Nitro-group frequencies (cm.$^{-1}$) of complexes of the type* $[Co(en)_2(NO_2)_2]X$.

	trans-*Isomers*			*cis*-Isomers			
X	ν_3	ν_1	ν_2	ν_3	ν_1	ν_1	ν_2
NO_3	1433 s	1348 sh 1319 s	828 s	1425 s 1404 s	1344 s	1314 s	830 s 821 s
NO_2	1435 s	1335 s 1318 s	823 s	1418 s 1404 s	1348 s	1314 s	828 s 821 s
I	1418 1404 s	1321 s 1305 s	816 s	—	—	—	—
Cl	1414 s	1325 s 1312 sh	819 s	1422 s 1397 sh	1344 s	1323 wsh 1312 s 1304 wsh	832 s 819 s
SCN	1422 s	1332 s 1314 sh	824 s	1416 s 1395 sh	1344 s	1316 s	827 s 821 s

In Table 3 are listed the frequencies of the nitro-groups in the *cis*- and *trans*-isomers of a series of dinitrobisethylenediaminecobalt(III) complexes. The *trans*-isomers of the

dinitro-series have bands with the following ranges: ν_3, 1419 ± 16; ν_1, 1334 ± 14 and 1312 ± 7; ν_2, 822 ± 6 cm.$^{-1}$. The *cis*-isomers of the dinitro-series have bands with the ranges: ν_3, 1420 ± 5 and 1399 ± 5; ν_1, 1314 ± 2; ν_2, 829 ± 3 and 820 ± 1 cm.$^{-1}$. There is an additional band at 1346 ± 2 cm.$^{-1}$.

In the spectra of the *trans*-dinitro-complexes only one band was observed corresponding to ν_3, whereas in the case of the *cis*-isomers this band is split. The frequencies assigned to ν_3 and ν_2 for the *trans*-isomers were very similar to those obtained for the mononitro-complexes. ν_1 was split in the *trans*- but not in the *cis*-isomers. However, an extra band was observed in the spectra of the *cis*-isomers at about 1350 cm.$^{-1}$; this was reported [2] for the *cis*-dinitrotetramminecobalt(III) anion where it was stated to be a natural consequence of the lower symmetry.

The band arising from the bending vibration (ν_2) was split into two distinct peaks in the *cis*-dinitro-isomers with frequency ranges of 829 ± 3 and 820 ± 1 cm.$^{-1}$, as in the *cis*-platinous complexes previously described.

This splitting of ν_2 when two nitro-groups are in *cis*-positions to one another was also observed for the compounds given below:

$Na_2[Pd(NO_2)_4]$	848 s	825 s
$Na_2[RuNO(NO_2)_4OH],2H_2O$	837 vs	829 vs

Mathieu [6] examined the Raman spectra of two tetranitro- and two hexanitro-complexes of Group VIII metals and reported bands at 846 ± 1 and 833 ± 2 cm.$^{-1}$ for each of these compounds. The 827 cm.$^{-1}$ band of sodium nitropalladate falls outside this range, but this compound decomposed while being examined. The frequencies reported are listed below:

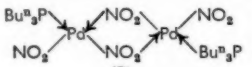
$Na_2[Pt(NO_2)_4]$	1412	1364	1325	847	835
$Na_2[Pd(NO_2)_4]$	—	—	—	—	827 *
$Na_3[Rh(NO_2)_6]$	1406	1380	1322	847	832
$Na_3[Ir(NO_2)_6]$	1408	1370	1327	846	835

* Decomposed during measurement.

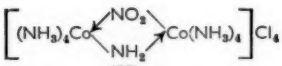
Bands appear in the regions expected for ν_3 and ν_1, and an extra band appears at 1372 ± 8 cm.$^{-1}$ as observed here for the *cis*-dinitro-isomers.

It appears therefore that, whenever two nitro-groups are in *cis*-relation to one another and attached to the same central metal atom, the band in the 820 cm.$^{-1}$ region is split and an extra band occurs in the 1350 cm.$^{-1}$ region. Sometimes one of the two bands observed here for ν_2 may be infrared-inactive; *e.g.*, only one peak is observed at 845 cm.$^{-1}$ in the spectrum of $Na_3[Co(NO_2)_6]$.

Complexes containing bridging nitro-groups. Infrared spectroscopy has been very valuable in establishing the existence of carbonyl (CO) [7] and thiocyanate (SCN) [8] bridging groups in metal co-ordination complexes. A few examples are known where the nitro-group functions as a bridging group between metal atoms, and we have examined two of these, *viz.*, dinitrobis(tri-n-butylphosphine)-$\mu\mu'$-dinitropalladium(II) (I) and bistetrammine-μ-nitro-μ-aminocobalt(III) chloride (II).



(I)



(II)

In Table 4 are given the frequencies of the absorption bands in the spectra of $[(PBu^n_3)_2Pd(NO_2)_2]$ and of the bridged complexes of palladium (chloro-, nitro-, and oxalato-bridges) in carbon tetrachloride and of cobalt(III) (nitro- and amido-, and peroxy- and amido-bridges) in potassium bromide discs.

[6] Mathieu, *J. Chim. phys.*, 1939, **36**, 271, 308.
[7] Sheline and Pitzer, *J. Amer. Chem. Soc.*, 1950, **72**, 1107.
[8] Chatt and Duncanson, *Nature*, 1956, **176**, 997; *J.*, 1958, 43.

The spectrum of the nitro-bridged palladium complex was measured in carbon tetrachloride solution in the sample beam, with the corresponding chloro-bridged complex in the reference beam of the double-beam spectrometer, thereby reducing the apparent absorption due to alkyl groups. The nitro-bridged complex was also run in opposition to the corresponding *trans*-dinitro-mononuclear complex to ascertain whether there was any absorption arising

TABLE 4. NO_2 *Frequencies (cm.*$^{-1}$*) of some bridged complexes.*

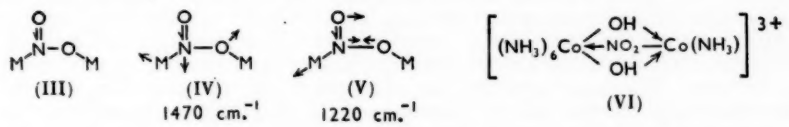
Compound	Bridged NO_2	NO_2	NO_2	Bridged NO_2
$(PBu^n_3)_2Pd_2(NO_2)_4$	1475 s	1421 s	1330 s	1238 s
$(PBu^n_3)_2Pd_2(C_2O_4)(NO_2)_2$		1429 s	1326 s	
$(AsBu^n_3)_2Pd_2Cl_2(NO_2)_2$		1421 s	1322 s	
$(PBu^n_3)_2Pd(NO_2)_2$(*trans*)		1414 sh *	1326 s	
		1395 b		

	Bridged NO_2	NH_2/NH_2	NH_2/NH_2	Bridged NO_2
$\left[(NH_3)_4Co\begin{smallmatrix}\diagup NO_2 \diagdown \\ \diagdown NH_2 \diagup\end{smallmatrix}Co(NH_3)_4\right]Cl_4,H_2O$	1485	1340	1296	1183
$\left[(NH_3)_4Co\begin{smallmatrix}\diagup O_2 \diagdown \\ \diagdown NH_2 \diagup\end{smallmatrix}Co(NH_3)_4\right]Cl_4,4H_2O$		1332	1298	

* The splittings were observed by using a grating instrument

from the bridged nitro-group which was obscured by the terminal nitro-absorption bands. The asymmetric NO_2 stretching frequency of the mononuclear complex does not exactly cancel owing to a splitting of this band not present in the binuclear complex. No additional absorption was observed for the binuclear complex. By comparison with the spectrum of the corresponding mononuclear complex of palladium, it is clear that the bridged group is giving rise to absorption bands at 1472 ± 3 and 1230 ± 10 cm.$^{-1}$, the limits covering the use of different solvents (CCl_4 and $CHCl_3$).

The cobalt complexes showed absorption assigned to the nitro-bridging group at 1485 and 1183 cm.$^{-1}$, these being determined by comparison with the corresponding peroxy-bridged complex. It is noteworthy that no absorption characteristic of the peroxy-bridge was observed. The difference between the frequencies observed for the cobalt and the palladium complexes may be ascribed either to the use of potassium bromide discs, or to the fact that the cobalt complexes contain a five-membered ring system compared with the six-membered system in the palladium complexes.



In the esters of carboxylic acids absorption bands in the 1700 and 1200 cm.$^{-1}$ regions have been assigned to the stretching vibrations of the CO bonds, and by analogy we suggest that the structure of the bridging nitro-group has the form (III), the frequencies observed arising from the vibrations (IV) and (V). If the nitrogen atom alone were in the bridge then the NO_2 stretching frequencies would be expected to lie closer together. In agreement with this, Nakamoto, Fujita, and Murata [2] have recently assigned bands at 1516 cm.$^{-1}$ and 1200 cm.$^{-1}$ in the spectrum of the ion (VI) to vibrations of the bridging nitro-group. They also propose the same structure as we do for the bridging nitro-group.

EXPERIMENTAL

Determination of Spectra.—The infrared spectra were obtained with Grubb–Parsons double-beam or single-beam infrared spectrometers equipped with S3A monochromators and rock-salt

prisms. The mulling agents used were Nujol (2–15 μ) and hexachlorobutadiene. The latter was used for the region obscured by Nujol absorption bands. Solvents used were chloroform and carbon tetrachloride (1500—1200 cm.$^{-1}$) and acetone (830—800 cm.$^{-1}$).

The solid samples, with the exception of the bridged cobalt complexes which were examined in potassium bromide discs, were examined between rock-salt plates; in cases where it appeared likely that replacement of NO_2 by chloride from the rock-salt would occur, the plates used were coated with a fine film of polystyrene.[9]

Preparation of Compounds.—The nitro-complexes were prepared by established methods, and their configurations established by measuring their $\Delta\varepsilon/f$,[10] where $\Delta\varepsilon$ = the increment in dielectric constant due to the substance in dilute benzene solution and f = the mole-fraction of the substance. The products are colourless unless otherwise stated.

trans-*Dinitro-(4-n-pentylpyridine)platinum.* The dichloro-analogue[11] (2 g.) and sodium nitrite (2 g.) in methanol (75 c.c.) were boiled under reflux for 4 hr. The almost colourless solution was evaporated to dryness, and the *product* washed with water, dried, and recrystallised from ethanol, to give plates, m. p. 163—163·5°, $\Delta\varepsilon/f = 4{\cdot}5$ (yield 82%) (Found: C, 41·3; H, 5·5; N, 9·7. $C_{20}H_{30}O_4N_4Pt$ requires C, 41·0; H, 5·2; N, 9·6%).

trans-*Dinitrobis(tri-n-butylphosphine)platinum.* Potassium chloroplatinite (2·1 g.) and sodium nitrite (2 g.) in water (50 c.c.) were shaken until the solution became pale yellow. Tri-n-butylphosphine (2·0 g.) was then added in a nitrogen atmosphere, and the mixture shaken for 20 hr. The resulting white precipitate was removed and dried. Three recrystallisations from aqueous methanol gave the *product* as prisms, m. p. 147·5—148·5°, $\Delta\varepsilon/f = 3{\cdot}4$ (yield 51%) (Found: C, 41·9; H, 8·1; N, 3·9. $C_{24}H_{54}O_4N_2P_2Pt$ requires C, 41·7; H, 7·9; N, 4·0%).

trans-*Dinitrobis(tri-n-butylarsine)platinum* was similarly prepared and twice recrystallised from aqueous ethanol to give plates, m. p. 102·5—103° (yield 46%), $\Delta\varepsilon/f = 3{\cdot}5$ (Found: C, 37·0; H, 7·3; N, 3·5. $C_{24}H_{54}O_4N_2As_2Pt$ requires C, 37·0; H, 7·0; N, 3·6%).

trans-*Dinitrobis(di-n-butyl sulphide)platinum.* Hydrated sodium chloroplatinite (2 g.) in methanol (25 c.c.) was added to sodium nitrite (1·2 g.) in methanol (50 c.c.), and the solution kept until it had turned yellow. Di-n-butyl sulphide (1·7 c.c.) was then added. After 24 hr. this solution was evaporated to dryness; the residual *product* (12%), recrystallised from methanol, decomposed at 194·5—196° and had $\Delta\varepsilon/f = 12{\cdot}1$ (Found: C, 33·4; H, 6·5; N, 4·4. $C_{16}H_{36}O_4N_2S_2Pt$ requires C, 33·15; H, 6·3; N, 4·8%).

trans-*Dinitrobis(di-n-propyl selenide)platinum* was prepared in the same way as its tri-n-butylphosphine analogue but with only 4 hours' shaking and recrystallisation from methanol; it had m. p. 173—174° (sinters 170°) (yield 63%), $\Delta\varepsilon/f = 13{\cdot}2$ (Found: C, 23·6; H, 4·6; N, 4·4. $C_{12}H_{28}O_4N_2PtSe_2$ requires C, 23·3; H, 4·6; N, 4·5%).

trans-*Dinitrobis(di-n-propyl telluride)platinum* was prepared similarly. The pale orange product on extraction with hot light petroleum (b. p. 60—80°) gave a solution which on cooling deposited pale yellow needles, m. p. 46—47° (41%) (Found: C, 20·3; H, 4·0; N, 4·3. $C_{12}H_{28}O_4N_2PtTe_2$ requires C, 20·2; H, 3·95; N, 3·9%).

cis-Dinitrobis(tri-n-butylphosphine)platinum was prepared through the corresponding sulphate in a manner similar to that by which Jensen[12] prepared its ethyl analogue.

Sulphatobis(tri-n-butylphosphine)platinum. The dichloro-analogue (2 g.) and silver sulphate (10 g., 10 equiv.) were shaken in methanol (75 c.c.) for 20 hr. The mixture was filtered, and the filtrate taken to dryness. The residue on repeated recrystallisation from ethyl acetate gave the *complex* as needles (0·9 g.), m. p. 175—176·5° (Found: C, 41·2; H, 7·8. $C_{24}H_{54}O_4SP_2Pt$ requires C, 41·4; H, 7·8%).

cis-*Dinitrobis(tri-n-butylphosphine)platinum.* The sulphato-compound (0·7 g.) in methanol (20 c.c.) was treated with sodium nitrite (0·3 g.) in water (4 c.c.), and the mixture boiled under reflux for 15 min., then filtered. The residue was extracted with methanol (10 c.c.), and the combined filtrates were evaporated to dryness. The residue, twice recrystallised from methanol, gave pale cream leaflets (0·6 g.), m. p. 140·5—142°, $\Delta\varepsilon/f = 280$ (Found: C, 41·9; H, 8·0; N, 4·0%).

cis-Dinitrobis(di-n-butyl sulphide)platinum, prepared as described by Löndahl[13] from

[9] Gatehouse, *Chem. and Ind.*, 1957, 1351.
[10] Chatt and Wilkins, *J.*, 1953, 70.
[11] Ahrland and Chatt, *J.*, 1957, 1379.
[12] Jensen, *Z. anorg. Chem.*, 1936, **229**, 225.
[13] Löndahl, see Gmelin, "Handbuch der Anorganischen Chemie," Platinum, Part D, System No. 68, p. 318.

$(Bu^n_2S)_2PtSO_4$ and crystallised from aqueous ethanol, had m. p. 199° (decomp.) (softened over a wide range) (Löndahl gave m. p. 193°), $\Delta\varepsilon/f = 147{\cdot}0$ (Found: C, 33·0; H, 6·5; N, 4·8%).

trans-*Dinitrobis*-(*4-n-pentylpyridine*)*palladium*. Hydrated sodium chloropalladite (3 g.) and sodium nitrite (3 g.) in methanol (*ca.* 75 c.c.) were treated with 4-n-pentylpyridine (3 c.c.). The mixture was taken to dryness at 100°, and the residue extracted with water, leaving a yellow residual *complex* which recrystallised from acetone as yellow plates, m. p. 131—132·5° (74%), $\Delta\varepsilon/f = 5{\cdot}6$ (Found: C, 48·5; H, 6·1. $C_{20}H_{30}O_4N_4Pd$ requires C, 48·3; H, 6·1%).

trans-Dinitrobis(tri-n-butylphosphine)palladium,[12] obtained analogously to Mann and Purdie's preparation of its n-propyl homologue,[14] had m. p. 141—142°, $\Delta\varepsilon/f = 3{\cdot}5$ (Found: Pd, 17·6; C, 47·7; H, 9·0; N, 4·4. Calc. for $C_{24}H_{54}O_4N_2P_2Pd$: Pd, 17·7; C, 47·8; H, 9·0; N, 4·65%).

trans-Dinitrobis(tri-n-butylarsine)palladium,[12] similarly prepared, had m. p. 96°, $\Delta\varepsilon/f = 3{\cdot}7$ (Found: Pd, 15·4; C, 42·0, 41·55; H, 7·8. Calc. for $C_{24}H_{54}O_4N_2As_2Pd$: Pd, 15·4; C, 41·7; H, 7·9%).

trans-Dinitrobis(di-n-butyl sulphide)palladium,[15] prepared in similar manner to its platinum analogue, had m. p. 171—172°, $\Delta\varepsilon/f = 9{\cdot}3$ (Found: Pd, 21·7; C, 39·0; H, 7·35; N, 5·5. Calc. for $C_{16}H_{36}O_4N_2S_2Pd$: Pd, 21·7; C, 39·1; H, 7·4; N, 5·5%).

trans-*Dinitrobis*(*di-n-propyl selenide*)*palladium* was prepared in the same way as its platinum analogue and recrystallised from methanol as yellow leaflets, m. p. 145—146° (gradual softening) (72%), $\Delta\varepsilon/f = 10{\cdot}7$ (Found: C, 27·3; H, 4·9; N, 5·6. $C_{12}H_{28}O_4N_2PdSe_2$ requires C, 27·3; H, 5·3; N, 5·3%).

trans-*Dinitrobis*(*di-n-propyltelluride*)*palladium* was similarly prepared from potassium chloropalladite (2·3 g.), potassium nitrite (3 g.), and di-n-propyl telluride (4 g.). The reddish product (4·9 g.) was extracted with boiling light petroleum (b. p. 60—80°) (200 c.c.), and the filtrate, on cooling, deposited orange needles, m. p. 58—59° (with premature softening) (1·5 g.) (Found: C, 23·1; H, 4·5; N, 4·55. $C_{12}H_{28}O_4N_2PdTe_2$ requires C, 23·0; H, 4·5; N, 4·5%).

Dinitrobis(tri-n-butylphosphine)-$\mu\mu'$-dinitrodipalladium [14] had m. p. 138° (Found: Pd, 26·2; C, 35·7; H, 6·9; N, 7·1. Calc. for $C_{24}H_{54}O_8N_4P_2Pd_2$: Pd, 26·6; C, 35·9; H, 6·8; N, 7·0%). Dinitrobis(tri-n-butylphosphine)-μ-oxalatopalladium [14] had m. p. 200—205° (decomp.) (Found: Pd, 26·65; C, 39·0; H, 6·8. Calc. for $C_{26}H_{54}O_6N_2P_2Pd_2$: Pd, 26·7; C, 39·1; H, 6·8%).

Dinitrobis(*tri-n-butylarsine*)-$\mu\mu'$-*dichlorodipalladium* was prepared following Mann and Wells's directions [16] but by using Bu^n_3As in place of Me_3As; it had m. p. 124° (Found: Pd, 24·2; C, 32·8; H, 6·15. $C_{24}H_{54}O_4N_2Cl_2As_2Pd_2$ requires Pd, 24·3; C, 32·8; H, 6·2%).

Bistetrammine-μ-nitro-μ-aminodicobalt(III) chloride monohydrate was prepared as described by Werner and Baselli [17] (Found: Co, 24·9; Cl, 29·7. Calc. for $H_{28}O_3N_{10}Cl_4Co_2$: Co, 24·8; Cl, 29·8%), and bistetrammine-μ-peroxy-μ-aminocobalt(III) chloride tetrahydrate as described by Werner [18] (Found: Co, 23·1; Cl, 27·3. Calc. for $H_{34}O_6N_9Cl_4Co_2$: Co, 22·9; Cl, 27·5%).

The following compounds were prepared as described by Werner: [19] *trans*-$[Co(en)_2(NO_2)SCN]SCN$ (Found: Co, 17·3. Calc. for $C_6H_{16}O_2N_7S_2Co$: Co, 17·3%). *cis- and trans*-$[Co(en)_2(NO_2)SCN]Cl$ (Found: *cis*-isomer, Co, 18·4; *trans*-isomer, Co, 18·2. Calc. for $C_5H_{16}O_2N_6ClSCo$: Co, 18·4%). *cis*- and *trans*-$[Co(en)_2(NO_2)SCN]NO_2$ (Found: *cis*-isomer, Co 18·1; *trans*-isomer, Co, 17·6. Calc. for $C_5H_{16}O_4N_7SCo$: Co, 17·9%). *trans*-$[Co(en)_2(NO_2)Cl]SCN$ (Found: Co, 19·0. Calc. for $C_5H_{16}O_2N_6SClCo$: Co, 18·4%).

cis-$[Co(en)_2(NO_2)Cl]NO_2$ was prepared as described by Werner and Gerb [20] (Found: Co, 19·3. Calc. for $C_4H_{16}O_4N_6ClCo$: Co, 19·2%), as was *cis*-$[Co(en)_2(NO_2)Cl]Cl$ (Found: Co, 19·9. Calc. for $C_4H_{16}O_2N_5Cl_2Co$: Co, 19·9%).

cis-$[Co(en)_2(NO_2)_2]NO_3$ was prepared according to Werner and Humphrey,[21] and from it the *trans*-isomer was prepared following Werner's instructions [19] (Found: *cis*-isomer, Co, 17·5; *trans*-isomer, Co, 17·5. Calc. for $C_4H_{16}O_7N_7Co$: Co, 17·7%).

cis-$[Co(en)_2(NO_2)_2]NO_2$ was prepared by a recorded method,[22] and the *trans*-isomer according

[14] Mann and Purdie, *J.*, 1936, 873.
[15] Mann and Purdie, *J.*, 1935, 1549.
[16] Mann and Wells, *J.*, 1938, 702.
[17] Werner and Baselli, *Z. anorg. Chem.*, 1898, **16**, 150.
[18] Werner, *Ber.*, 1907, **40**, 4609.
[19] Werner, *Annalen*, 1912, **386**, 1—272.
[20] Werner and Gerb, *Ber.*, 1901, **34**, 1739.
[21] Werner and Humphrey, *Ber.*, 1901, **34**, 1719.
[22] *Inorg. Synth.*, 1953, **4**, 177.

to Werner and Humphrey [21] (Found: *cis*-isomer, Co, 18·45; *trans*-isomer, Co, 18·4. Calc. for $C_4H_{16}O_6N_7Co$: Co, 18·6%).

trans-$[Co(en)_2(NO_2)_2]I$ was prepared from the *trans*-nitrate by treating a solution of the latter with a warm solution of potassium iodide; the crystalline product which formed was filtered off and dried in a desiccator over sulphuric acid (Found: Co, 14·7. Calc. for $C_4H_{16}O_4N_6ICo$: Co, 14·8%).

cis- and *trans*-$[Co(en)_2(NO_2)_2]Cl$ were prepared by passing the *cis*- and *trans*-nitrate complexes respectively through Amberlite I.R.A.-400 (OH^- form). The eluant contained the hydroxyl complex, and was neutralised with hydrochloric acid and evaporated over concentrated sulphuric acid in a vacuum-desiccator to crystallisation (Found: *cis*-isomer, Co, 19·0; *trans*-isomer, Co, 19·1. Calc. for $C_4H_{16}O_4N_6ClCo$: Co, 19·2%). *cis*- and *trans*-$[Co(en)_2(NO_2)_2]SCN$ were prepared by Werner's method [19] (p. 199) (Found: *cis*-isomer, Co, 17·8; *trans*-isomer, Co, 17·8. Calc. for $C_5H_{16}O_4N_7SCo$: Co, 17·9%).

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818. *Acid-catalysed Rearrangements of Alkyl Aryl Ethers. Part I. Rearrangement of Butyl Phenyl Ethers with Aluminium Chloride.*

By M. J. S. Dewar and N. A. Puttnam.

Rearrangements of n- and s-butyl phenyl ethers in presence of aluminium chloride have been studied and the products shown to be identical. The products have been compared with those obtained by alkylation of phenol with n- and s-butyl chloride in similar conditions, and conclusions are drawn concerning the mechanism of the rearrangements. A number of n- and s-butyl derivatives of phenol have been synthesised as reference compounds.

The rearrangement of alkyl aryl ethers to alkylphenols in presence of aluminium chloride was first noticed in 1892 by Hartmann and Gattermann,[1] who obtained in this way from isobutyl phenyl ether a product which they described as *p*-isobutylphenol; since then very little work has been published on reactions of this kind, with the notable exception of a series of papers by Smith in 1933—1934.

Smith found [2] that the rearrangement product isolated by Hartmann and Gattermann was, not *p*-isobutylphenol, but *p*-t-butylphenol, and they obtained the same compound by treating t-butyl phenyl ether with aluminium chloride. Smith therefore concluded that the reaction was intermolecular, involving removal of the butyl residue (presumably as isobutene or a butyl chloride) followed by Friedel–Crafts alkylation of the phenol simultaneously formed. This idea seemed to be confirmed by similar reactions in which alkyl groups migrated to foreign nuclei. Smith was able to isolate [3] 2,4-di-isopropylphenol in 10% yield, together with a mixture (50%) of *o*- and *p*-isopropylphenol, after rearrangement of isopropyl phenyl ether; and when the same ether was treated with aluminium chloride in presence of diphenyl ether, intermolecular migration of the alkyl group occurred.[4]

However, Smith also claimed [5] that rearrangement of n-butyl phenyl ether with aluminium chloride gave a mixture of *o*- and *p*-n-butylphenol. This would be difficult

[1] Hartmann and Gattermann, *Ber.*, 1892, **25**, 3531.
[2] Smith, *J. Amer. Chem. Soc.*, 1933, **55**, 3718.
[3] *Idem, ibid.*, p. 849.
[4] *Idem, ibid.*, 1934, **56**, 717.
[5] *Idem, ibid.*, p. 1419.

to explain in terms of an intermolecular mechanism; for any alkylation of the Friedel–Crafts type should involve intermediate alkyl cations, and the n-butyl ion would immediately rearrange. It is, of course, known that such alkylations with n-alkyl chlorides invariably give rearranged products.

It is true that the analytical techniques available in Smith's time were scarcely adequate for dealing with the complex mixtures formed in reactions of this type; but his claim that the analogous rearrangement of s-butyl phenyl ether gave a mixture of s-butylphenols certainly seemed to indicate a difference between the rearrangement products in the two cases.

We therefore decided to re-examine the rearrangements of n- and s-butyl phenyl ether, using modern analytical techniques, and to compare the products with those formed by Friedel–Crafts alkylation of phenol in comparable conditions.

Preparation of Reference Compounds.—Since we intended to carry out our analyses by infrared spectroscopy, we had first to synthesise pure samples of all the possible rearrangement products.

The isomeric n-butylphenols were prepared (cf. Klages [6]) by addition of n-propylmagnesium iodide to the appropriate methoxybenzaldehyde, dehydration to the butenylanisole, reduction to n-butylanisole, and demethylation.

The three s-butylphenols were prepared in an analogous manner by Grignard reactions between the appropriate methoxyphenylmagnesium bromide and ethyl methyl ketone, followed again by dehydration, reduction, and demethylation; and 2,4-di-s-butylphenol was obtained likewise from 2-methoxy-5-s-butylphenylmagnesium bromide.

2,6-Di-s-butylphenol, which had not previously been described, was obtained by *ortho*-Claisen rearrangement of the but-2-enyl ether [7] of *o*-s-butylphenol, followed by reduction.

2,4,6-Tri-s-butylphenol was prepared in an analogous way from *p*-s-butylphenol, by two successive rearrangements.

The infrared spectra of all these compounds have been published in the D.M.S. records.

Rearrangements and Alkylations.—Smith [2-5] gave no indication of the temperature at which his rearrangements were carried out, apart from a statement that the heat evolved on adding aluminium chloride to the ether was absorbed in an external cooling bath. In the rearrangements and alkylations reported in this paper the aluminium chloride was added in small portions with cooling to the ether, or to the mixture of phenol or anisole with butyl chloride, during 30 minutes, with external cooling so that the temperature remained in the range 15—25°. The reactions were carried out both with equimolecular amounts of aluminium chloride, and with half-molar amounts. The products were analysed by means of infrared spectra measured for carbon tetrachloride solutions (2% w/w) on a Grubb–Parsons G.S. 2A double-beam grating spectrometer over the range 900—1120 cm.$^{-1}$.

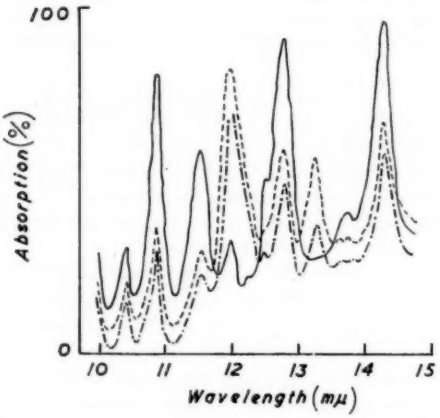
Results.—The products from the alkylation of phenol, or rearrangement of butyl phenyl ether, all consisted of mixtures of all three s-butylphenols, a mixture of di-s-butylphenols, and phenol. No n-butylphenols were detected in the products from n-butyl chloride and phenol, or from n-butyl phenyl ether. Smith's claim [5] that n-butylphenols are formed in the latter reaction must therefore be rejected. Rearrangement cannot follow migration since *o*-n-butylphenol was unaffected by aluminium chloride in the conditions of the reaction.

The formation of *m*-alkylphenols by rearrangement of alkyl aryl ethers has not previously been reported. We were unable to isolate *m*-s-butylphenol from our products, but its presence in small amounts (*ca.* 2%) was definitely indicated in all cases by the spectra. Fractional distillation of the crude rearrangement product gave a fraction in which the concentration of *m*-s-butylphenol was about 15%, and there its presence was established unambiguously by the spectrum (see the Figure).

[6] Klages, *Ber.*, 1904, **37**, 3987.
[7] Claisen and Tietze, *Ber.*, 1926, **59**, 2344.

The mixture of dialkylphenols consisted of two isomers. One was 2,4-di-s-butylphenol. The other, which was not the 2,6-isomer, was not definitely identified. Since, however, the same compound was formed by rearrangement of s-butyl *p*-s-butylphenyl ether, it was probably 3,4-di-s-butylphenol, whose formation would not be surprising. Secondary alkyl cations are known [8] to show low selectivity, and so alkylation of *p*-s-butylphenol by s-butyl cations could well give comparable amounts of 2,4- and 3,4-di-s-butylphenol. The infrared spectrum of the unknown compound was found by difference, the spectrum of its mixture with 2,4-di-s-butylphenol being balanced against that of a solution of 2,4-di-s-butylphenyl itself.

The only other product we detected was 2,4,6-tri-s-butylphenol, which was formed in small amounts in the rearrangement of phenyl s-butyl ether.



Infrared spectral evidence for the presence of m-*s-butylphenol in the rearrangement product from phenyl s-butyl ether*: m-*s-butylphenol* (——); *an authentic mixture of s-butylphenols containing* 15% *of the* m-*isomer* (– – –); *one fraction from the rearrangement product* (— · — · —).

Table 1 records the products formed by rearrangement of n- and s-butyl phenyl ether under various conditions; Table 2 records the products formed in comparable alkylations of phenol.

TABLE 1. *Rearrangements in the presence of aluminium chloride at* 15—20° (*yields in moles* % *and* ortho/para *ratios*.

Ether	$AlCl_3$ (mol.)	Time (hr.)	PhOH	s-Butylphenols *o*-	*m*-	*p*-	Di-s-butyl phenols	*o*- : *p*- Ratio
Bu^n	1·0	36	30·4	11·2	2·0	34·5	16·6	0·325
	1·0	48	27·3	14·4	1·8	44·1	10·5	0·328
	0·5	70	13·5	11·3	0·7	14·5	Trace	0·780
	0·5	72	11·2	14·6	0·8	19·2	Trace	0·760
Bu^s	1·0	24	23·4	12·5	2·0	51·5	7·1	0·243
	0·5	24	28·5	14·5	2·0	44·0	8·5	0·330
	0·5	24	33·7	14·0	1·7	39·1	9·4	0·358
	1·0	24	24·0	12·7	2·4	48·9	9·3	0·260

TABLE 2. *Alkylation of phenol with n- and s-butyl chloride in presence of aluminium chloride* (*mol.*) *at* 15—20% (*yields in moles* % *and* ortho/para *ratios*).

Alkylating agent	Time (hr.)	PhOH	s-Butylphenols *o*-	*m*-	*p*-	Di-s-butyl-phenols	*o*- : *p*- Ratio
Bu^nCl	60	23·0	8·7	1·9	43·4	13·2	0·200
Bu^sCl	36	25·9	8·7	2·0	42·3	13·3	0·206
	28	29·3	7·6	2·0	38·8	16·3	0·196
	24	25·2	9·3	2·0	46·5	10·4	0·200

In this work we also examined the alkylation of anisole by n- and s-butyl chloride; the results are shown in Table 3. Each monoalkyl fraction was shown to contain all three

[8] Brown and Nelson, *J. Amer. Chem. Soc.*, 1953, **75**, 6292.

isomeric s-butylanisoles, but no n-butylanisoles. No attempt was made to analyse the products quantitatively.

TABLE 3. *Products (moles %) from alkylation of anisole with n- and s-butyl chloride at 15—20°.*

Reagent	Time (hr.)	PhOH	PhOMe	Mono-s-butyl-anisoles	Di-s-butyl-anisoles
Bu^nCl	60	3·3	58·7	12·4	1·8
Bu^sCl	48	4·9	18·5	40·4	13·6

Discussion.—If the rearrangements are intermolecular, one would expect (*a*) that n-butyl would rearrange to s-butyl during migration; (*b*) that rearrangement of n-butyl and s-butyl phenyl ethers would give identical products; (*c*) that rearrangement of either butyl ether would give the same products as alkylation of phenol under similar conditions, with either n- or s-butyl chloride.

The first of these conditions certainly seems to be met; we could not detect n-butylphenols in the rearrangement products of n-butyl phenyl ether.

The rearrangement products of n-butyl and s-butyl phenyl ethers under comparable conditions were similar but not identical (see Table 1); rearrangement of the n-butyl ether gave a larger proportion of *o*-butylphenol. The difference was more marked with half-molar proportions of catalyst.

Comparison of Tables 1 and 2 shows that the products from the rearrangements and and alkylations, though similar, were again not identical. The proportion of *o*-butylphenol in the alkylation products was much less than in the rearrangement products.

That these differences were real is indicated by the constancy of the *ortho*/*para* ratios in the various alkylation products; all the alkylation products gave very similar analyses. It therefore seems unlikely that the rearrangements involve only a simple intermolecular process, as proposed by Smith.[2] The mechanism of these reactions will be considered in detail in a later paper of this series (cf. ref. 9); there it will be shown that two distinct reactions are probably involved, one a heterogeneous intermolecular reaction on the surface of the solid catalyst, the other a homogeneous intramolecular rearrangement catalysed by the aluminium chloride dissolved in the ether.

One point should be emphasised in this connexion; since in no case was a n-butylphenol detected after rearrangement of n-butyl phenyl ether, either the n-butyl group must isomerise during migration, or the n-butyl ether must isomerise to s-butyl ether before rearrangement. In an experiment where the rearrangement of n-butyl phenyl ether was interrupted before completion, no trace of s-butyl phenyl ether could be detected in the unchanged ether recovered. Therefore, either the n-butyl ether is not isomerised before rearrangement, or the s-butyl ether formed from it rearranges as fast as it is formed. The latter is not impossible: rearrangement of s-butyl phenyl ether is certainly very much faster than that of the n-isomer.

EXPERIMENTAL

Microanalyses were carried out by the Microanalytical Laboratory, Imperial College, South Kensington, London, S.W.7, and by Alfred Bernhardt, Max-Planck-Institut, Mülheim Germany.

Alkyl phenyl ethers, prepared from phenol, the alkyl bromide, and potassium hydroxide according to the method of Niederl and Natelson [10] were: phenyl s-butyl ether, b. p. 195°, n_D^{18} 1·4962; n-butyl phenyl ether, b. p. 207°, n_D^{17} 1·4984; s-butyl *p*-s-butylphenyl ether, b. p. 238°, n_D^{19} 1·4925; and n-butyl *p*-s-butylphenyl ether, b. p. 236°, n_D^{17} 1·4927.

Aryloxyacetic acids were prepared by refluxing the phenol (1 g.) in water (30 ml.) with potassium hydroxide (4 g.) and chloroacetic acid (1·5 g.) for 1 hr. and were recrystallised from water or light petroleum (b. p. 60—80°).

[9] Dewar and Puttnam, *Proc. Chem. Soc.*, 1959, 58.
[10] Niederl and Natelson, *J. Amer. Chem. Soc.*, 1931, **53**, 1928.

Phenylurethanes were prepared according to Steinkopf and Hopner's procedure [11] and recrystallised from light petroleum (b. p. 60—80°).

o-*n-Butylphenol.*—*o*-Anisaldehyde (54·5 g.) in dry ether (200 ml.) was added to a Grignard reagent prepared from magnesium (10·7 g.) and n-propyl iodide (304 g.) in dry ether (250 ml.). Next day the complex was hydrolysed, the ether layer evaporated, and the residue boiled under reflux for 18 hr. with acetic anhydride (500 ml.), then poured into water. The organic layer was collected and distilled; 1-*o*-methoxyphenylbut-1-ene was collected at 92—94°/1·5 mm. Hydrogenation over 5% palladised charcoal in ethanol at room temperature and 15 atm. gave *o*-n-butylanisole, b. p. 217°, n_D^{16} 1·5047 (Found: C, 80·6; H, 10·0. Calc. for $C_{11}H_{16}O$: C, 80·5; H, 9·8%). Demethylation with acetic acid and hydriodic acid gave *o*-n-butylphenol, b. p. 226°, n_D^{20} 1·5205 (aryloxyacetic acid, m. p. 101—102°; phenylurethane, m. p. 72°).

p-*n-Butylphenol.*—This was prepared in the same way as the *o*-isomer; 1-*p*-methoxyphenylbut-1-ene had b. p. 246°, n_D^{19} 1·5334; *p*-n-butylanisole had b. p. 88°/2 mm., n_D^{17} 1·5021; *p*-n-butylphenol had b. p. 245°, n_D^{15} 1·5202 (Found: C, 80·3; H, 9·6%) (aryloxyacetic acid, m. p. 83·5—84·5°; phenylurethane, m. p. 113—114°).

o-*s-Butylphenol.*—This was prepared in an analogous manner to the n-butylphenols, starting with the Grignard reagent from *o*-bromoanisole and ethyl methyl ketone; 2-*o*-methoxyphenylbut-2-ene had b. p. 219°, n_D^{17} 1·5316 (Found: C, 81·6; H, 8·9. Calc. for $C_{11}H_{14}O$: C, 81·5; H, 8·7%); *o*-s-butylanisole had b. p. 51°/0·4 mm., n_D^{17} 1·5052; *o*-s-butylphenol had m. p. 18°, b. p. 223°, n_D^{20} 1·5225 (aryloxyacetic acid, m. p. 112°; phenylurethane, m. p. 85°).

p-s-Butylphenol was prepared likewise; 2-*p*-methoxyphenylbut-2-ene had b. p. 233°, n_D^{17} 1·5478; *p*-s-butylanisole had b. p. 219°, n_D^{16} 1·5031; *p*-s-butylphenol had m. p. 58·5—9·5° (phenylurethane, m. p. 103—105°; aryloxyacetic acid, m. p. 60°).

2,4-*Di-s-butylphenol.*—Bromination of *p*-s-butylphenol in carbon tetrachloride at room temperature gave 2-bromo-4-s-butylphenol, b. p. 83·5°/0·4 mm., n_D^{18} 1·5499, which with methyl sulphate gave 2-bromo-4-s-butylanisole, b. p. 101°/0·6 mm., n_D^{18} 1·5428. This was converted as above *via* 2,4-di-s-butylanisole, b. p. 66·7°/0·1 mm., n_D^{23} 1·4940, into 2,4-di-s-butylphenol, b. p. 259°, n_D^{20} 1·5063 (Found: C, 81·8; H, 10·8. Calc. for $C_{14}H_{22}O$: C, 81·5; H, 10·8%). No solid aryloxyacetic acid or phenylurethane could be obtained.

2,6-*Di-s-butylphenol.*—A solution of but-2-enyl *o*-s-butylphenyl ether [8] (6·6 g.) in diethylaniline (50 ml.) was boiled under reflux for 5 hr. When cold, the solution was poured into hydrochloric acid and extracted with light petroleum (b. p. 40—60°). The hydrocarbon layer was extracted with Claisen solution [potassium hydroxide (350 g.) in water (250 ml.), made up to 1 l. with methanol]; acidification and distillation gave 2-1′-methylallyl-6-s-butylphenol, b. p. 80°/0·3 mm., n_D^{16} 1·5200 (phenylurethane, m. p. 120—121°); reduction with hydrogen (3 atm.) over 10% palladised charcoal in ethanol gave 2,6-*di-s-butylphenol*, b. p. 255°, n_D^{19} 1·5080 (Found: C, 81·3; H, 10·5. $C_{14}H_{22}O$ requires C, 81·5; H, 10·8%). The phenylurethane had m. p. 124—125°.

2-1′-*Methylallyl*-4-*s-butylphenol.*—But-2-enyl bromide (20·3 g.) was added slowly to a solution of *p*-s-butylphenol (22·5 g.) in acetone (50 ml.) containing anhydrous potassium carbonate (20·7 g.). The mixture was stirred at room temperature for 12 hr., and then boiled under reflux for 3 hr. Water and light petroleum (b. p. 40—60°) were added, and the organic layer separated, washed with Claisen solution, dried ($MgSO_4$), and distilled, giving but-2-enyl *p*-s-butylphenyl ether, b. p. 92°/0·5 mm., n_D^{15} 1·5096. Rearrangement of the ether as before gave 2-1′-methylallyl-4-s-butylphenol, b. p. 94°/0·5 mm., n_D^{22} 1·5176 (phenylurethane, m. p. 82°).

2,4,6-*Tri-s-butylphenol.*—2-1′-Methylallyl-4-s-butylphenol was converted as above through but-2-enyl 2-1′-methylallyl-4-s-butylphenyl ether, b. p. 110°/0·3 mm., n_D^{20} 1·5106, into 2,6-di-1′-methylallyl-4-s-butylphenol, b. p. 104°/0·2 mm., n_D^{18} 1·5186. Hydrogenation gave 2,4,6-tri-s-butylphenol, b. p. 282°, n_D^{16} 1·4995 (Found: C, 82·1; H, 11·4. Calc. for $C_{18}H_{30}O$: C, 82·4; H, 11·5%). No solid phenylurethane was obtained.

Rearrangement of n-Butyl Phenyl Ether.—(a) n-Butyl phenyl ether (125 g., 0·832 mole) was placed in a flask, equipped with condenser, stirrer, thermometer pocket, and polythene aluminium chloride dropper,[12] and surrounded with an external cooling bath; anhydrous aluminium chloride (111·3 g., 0·834 mole) was then added slowly with stirring during 30 min. so that the temperature was maintained within the range 15—25°. The cooling bath was then removed and the mixture left at room temperature for 48 hr., during which the mixture became

[11] Steinkopf and Hopner, *J. prakt. Chem.*, 1926, **113**, 137.
[12] Puttnam, Ph.D. Thesis, London, 1958.

dark red and very viscous and hydrogen chloride was slowly evolved. The mixture was hydrolysed with ice and hydrochloric acid, then the oil which separated was extracted with ether. This ethereal solution was washed with water until neutral, dried ($MgSO_4$), and evaporated. The residue (116 g.) was completely soluble in Claisen solution and was analysed by infrared spectroscopy. Partial separation of the products was effected by extraction with 15% potassium hydroxide solution. The alkali-soluble material (67 g.) was fractionated through a 15 cm. Dixon gauze column to give three fractions. The first fraction, b. p. 55—60°/0·5 mm., gave a phenylurethane, m. p. 126° undepressed by *ON*-diphenylurethane. The second fraction, b. p. 65—75°/0·5 mm. (Found: C, 79·6; H, 9·5. Calc. for $C_{10}H_{14}O$: C, 80·0; H, 9·4%), was shown by spectroscopy to be a mixture of *o*- (27%), *m*- (15%), and *p*-s-butylphenol (57%). The last fraction, b. p. 81—83°/0·5 mm., solidified and was shown by comparison with authentic samples to be *p*-s-butylphenol. The alkali-insoluble material (38·6 g.) was separated into three fractions. Fraction (i), b. p. 75—83°/0·5 mm., gave an aryloxyacetic acid, m. p. 111° (mixed with *o*-s-butylphenoxyacetic acid, m. p. 112°). Fraction (ii), b. p. 86—97°/0·5 mm., was shown by its spectrum to be a mixture of *o*-s-butylphenol, 2,4-di-s-butylphenol, and an unknown component. Fraction (iii), b. p. 98—102°/0·5 mm. (Found: C, 81·3; H, 10·9. Calc. for $C_{14}H_{22}O$: C, 81·5; H, 10·8%), was shown by its spectrum to be a 1 : 1 mixture of 2,4-di-s-butylphenol and the unknown component referred to above. A spectrum of this component was obtained by comparing a 2% solution of this fraction with a 1% solution of 2,4-di-s-butylphenol.

(b) The rearrangement was repeated with n-butyl phenyl ether (90 g., 0·6 mole) and anhydrous aluminium chloride (40 g., 0·3 mole). The products were separated as described above and extracted with Claisen solution, leaving an insoluble residue (49 g.) which was shown by its spectrum to be solely unchanged n-butyl phenyl ether. The material (33 g.) soluble in Claisen solution was analysed spectroscopically.

Rearrangement of s-Butyl Phenyl Ether.—(*a*) s-Butyl phenyl ether (100 g., 0·67 mole) was treated as above with anhydrous aluminium chloride (88·9 g., 0·67 mole) at 17—21°. The mixture was left at room temperature for 24 hr. and the products were separated as above. The rearranged material (97·2 g.), which was completely soluble in Claisen solution, was analysed spectroscopically. The products were partly separated by extraction with 20% potassium hydroxide solution. The alkali-soluble material (75·9 g.) was fractionated. The first fraction gave a urethane, m. p. 126° undepressed by *ON*-diphenylurethane. The second fraction, b. p. 82—86°/1·5 mm., was found by its spectrum to be a mixture of *o*- (38%), *m*- (12%) and *p*-s-butylphenol (50%). The third fraction was shown by comparison with an authentic specimen to be *p*-s-butylphenol. The last fraction, b. p. 102—106°/1·0 mm., was a mixture of *p*-s-butylphenol, 2,4-di-s-butylphenol, and the unknown component. The alkali-insoluble material (18·3 g.) was also fractionated. Fraction (i), b. p. 82—88°/1·0 mm., gave an aryloxyacetic acid, m. p. 112° undepressed by *o*-s-butylphenoxyacetic acid. Fraction (ii), b. p. 96—101°/1·0 mm., was found by its spectrum to be a 3 : 2 mixture of 2,4-di-s-butylphenol and the unknown di-s-butylphenol. Fraction (iii) was similarly shown to be a mixture of these two components, together with 2,4,6-tri-s-butylphenol (10%).

(*b*) s-Butyl phenyl ether (52·5 g., 0·35 mole) was treated with anhydrous aluminium chloride (23·3 g., 0·175 mole) at 15—18°. After 24 hr. at room temperature the mixture was hydrolysed and the organic layer separated as above. Removal of the ether gave rearranged material (49·8 g.) which was completely soluble in Claisen solution and was analysed spectroscopically.

Alkylations of Phenol. (*a*) Aluminium chloride (133·4 g.) was added slowly to a stirred mixture of phenol (94·1 g.) and n-butyl chloride (92·6 g.), at 15—20°. After 60 hr. at room temperature, the product was worked up as above, giving a mixture of alkylphenols (154·3 g.) which was analysed spectroscopically.

(*b*) A similar reaction with s-butyl chloride gave a mixture of alkylphenols (151·2 g.) which was similarly analysed.

Rearrangement of s-Butyl p-*s-Butylphenyl Ether.*—Rearrangement of s-butyl *p*-s-butylphenyl ether (10·5 g., 0·05 mole) with aluminium chloride (6·8 g., 0·05 mole) gave a product which was separated into two fractions by treatment with 10% aqueous potassium hydroxide. The soluble fraction (3·7 g.) gave a phenylurethane which did not depress the m. p. of *N*-phenyl-*O*-s-butylphenylurethane. The insoluble part was fractionated; one fraction, b. p. 259°, n_D^{22} 1·5070, was shown by its spectrum to be a mixture of 2,4-di-s-butylphenol and the unknown di-s-butylphenol. Another fraction, b. p. 278°, n_D^{22} 1·5058, was a mixture of these two compounds with 2,4,6-tri-s-butylphenol.

Effect of Aluminium Chloride on o-n-Butylphenol.—Aluminium chloride (0·9 g.) was added to *o*-n-butylphenol (1 g.). After 48 hr. at room temperature, the mixture was hydrolysed and extracted with ether, and the ether extract was distilled. The spectrum of the product was identical with that of *o*-n-butylphenol.

Alkylations of Anisole. These reactions were carried out with molar proportions of aluminium chloride as before. The products were treated with Claisen solution; the soluble part in each case was phenol. The insoluble part was fractionally distilled. The first fraction consisted of anisole. The second (b. p. 218°) was shown by its spectrum to be a mixture of *o*- and *p*-s-butylanisole, with a trace of the *m*-isomer. The third fraction apparently consisted of dibutylanisoles (Found: C, 81·8; H, 11·1. Calc. for $C_{15}H_{24}O$; C, 81·8; H, 11·0%); the last of trialkylanisoles (Found: C, 82·3; H, 11·4. Calc. for $C_{19}H_{32}O$: C, 82·6; H, 11·6%).

We thank Mr. J. C. Hawkes, Monsanto Chemicals Ltd., for his helpful advice on the spectral analyses; in connexion with this and the following two papers, one of us (N. A. P.) thanks Brighton Education Committee for a maintenance grant, and the University of London for a Postgraduate Studentship.

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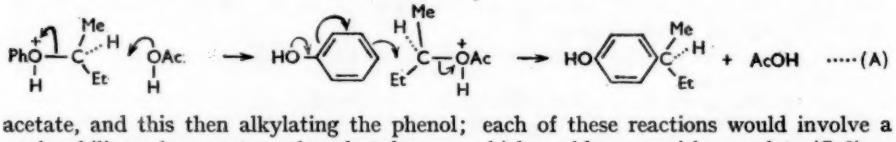
819. *Acid-catalysed Rearrangements of Alkyl Aryl Ethers. Part II.*[1] *Rearrangements in the Presence of Sulphuric–Acetic Acid Mixtures.*

By M. J. S. DEWAR and N. A. PUTTNAM.

Rearrangement of phenyl s-butyl ether in the presence of sulphuric acid in acetic acid has been studied and the products have been compared with those of alkylation of phenol with s-butyl alcohol under similar conditions. Crossed products have been isolated after rearrangement of a mixture of isopropyl *p*-tolyl and *p*-ethylphenyl s-butyl ether. A number of isopropyl and s-butyl derivatives of phenol have been synthesised as reference compounds.

PREVIOUS workers have favoured an intramolecular mechanism for the rearrangements of secondary alkyl ethers of phenols catalysed by sulphuric acid in acetic acid. Niederl and Natelson [2] reported that isopropyl phenyl ether gave *o*-isopropylphenol in over 50% yield, and no other alkyl- or dialkyl-phenol. Sprung and Wallis [3] obtained *o*-s-butylphenol as the only identifiable rearrangement product of phenyl s-butyl ether, although in only 8% yield. Since alkylation of phenol gives *p*-alkylphenol as the main product, these results suggested that the rearrangements of the phenyl ethers must be intramolecular.

Sprung and Wallis [3] also found that the rearrangement of optically active phenyl s-butyl ether gave optically active *o*-s-butylphenol; Diassi [4] later showed that the migration of the s-butyl group took place with retention of configuration, as would be expected if the rearrangement were intramolecular. It is true that retention of configuration might be observed in a two-step intermolecular process, the s-butyl group being removed as s-butyl



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acetate, and this then alkylating the phenol; each of these reactions would involve a nucleophilic replacement on the s-butyl group which could occur with complete (S_N2) or partial (S_Ni) inversion (cf. reactions A).

[1] Part I, preceding paper.
[2] Niederl and Natelson, *J. Amer. Chem. Soc.*, 1931, **53**, 1928.
[3] Sprung and Wallis, *ibid.*, 1934, **56**, 1715.
[4] Diassi, personal communication.

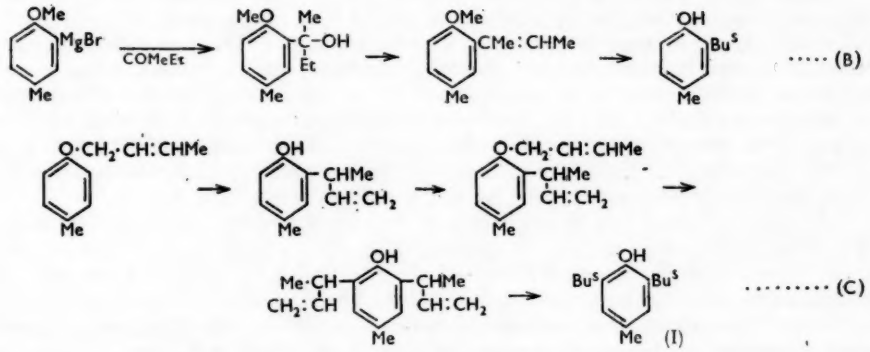
This possibility was excluded by Gilbert and Wallis [5] who showed that the intermolecular s-butylation of *p*-cresol by optically active mesityl s-butyl ether gave racemic 4-methyl-2-s-butylphenol, whereas rearrangement of optically active s-butyl *p*-tolyl ether gave optically active 4-methyl-2-s-butylphenol.

Gilbert and Wallis [5] also claimed that rearrangement of a mixture of isopropyl phenyl ether and s-butyl *p*-tolyl ether gave only isopropylphenol and s-butyl-*p*-cresol; if the rearrangement had been intermolecular, one would have expected some s-butylphenol and isopropyl-*p*-cresol to be formed.

These arguments are, however, by no means conclusive. The first and third rest on the failure to isolate certain compounds from complex products; the analytical methods available at the time were inadequate. Moreover the rates of rearrangement of an alkyl phenyl and an alkyl *p*-tolyl ether may differ greatly; in this case a mixture of the two could rearrange independently, even if each rearrangement were intermolecular. The argument based on retention of optical activity would be more convincing if retention were complete; the rotation reported by Sprung and Wallis [3] for *o*-s-butylphenol ($[\alpha]_D$ 4·77°) corresponds to an optical purity of 26·3%, based on the value ($[\alpha]_D$ 18·1°) quoted by Hawthorne and Cram [6] for the pure stereoisomer. Intramolecular rearrangements involving migration of optically active alkyl groups normally take place with complete retention of configuration.

We therefore re-examined the rearrangement of phenyl s-butyl ether, using modern analytical techniques, and also the rearrangement products from a mixture of isopropyl *p*-tolyl ether and *p*-ethylphenyl s-butyl ether. Crossed products would certainly be expected in the latter reaction if the rearrangements were intermolecular, since the electronic effects of methyl and ethyl substituents are similar.

The isopropyl and s-butyl derivatives of *p*-cresol and *p*-ethylphenol were prepared as were their analogues in Part I [1] (*e.g.*, by route B). 4-Methyl-2,6-di-s-butylphenol (I) was prepared by the method used [1] for the corresponding phenol derivative (C).



Results.—Rearrangements were carried out with molar amounts of concentrated sulphuric acid in a fourfold excess of glacial acetic acid for 2·5 hr. at 108—125°. The phenolic products were analysed by infrared spectroscopy of solutions in carbon tetrachloride (2% w/w) on a Grubb-Parsons G.S. 2A double-beam grating spectrometer over the range 900—1120 cm.$^{-1}$.

The main products from the rearrangement of phenyl s-butyl ether and the alkylation of phenol by s-butyl alcohol were butene, phenol, and sodium hydroxybenzenesulphonate, while the yields of s-butylphenols were quite small (8—12%). These results were in agreement with those obtained by Sprung and Wallis.[3] However, the phenolic fraction

[5] Gilbert and Wallis, *J. Org. Chem.*, 1940, **5**, 184.
[6] Hawthorne and Cram, *J. Amer. Chem. Soc.*, 1952, **74**, 5859.

was a mixture of *o*-, *m*-, and *p*-s-butylphenol together with 2,4-di-s-butylphenol; it resembled quite closely the corresponding products obtained [1] by using aluminium chloride as catalyst.

The presence of the *m*- and the 2,4-isomer was clearly indicated by the infrared spectrum; the *p*-isomer was characterised by its phenylurethane. The only other products identified were butyl and phenyl acetate and a mixture of hydroxyacetophenones.

Table 1 records the products formed by rearrangement of phenyl s-butyl ether; Table 2 records the products formed in comparable alkylations of phenol.

TABLE 1. *Rearrangements in sulphuric–acetic acid.*

			s-Butylphenol				
C_4H_8	PhOH	Na salt	*o*-	*m*-	*p*-	2,4-$Bu^s_2C_6H_3$·OH	*ortho*/*para* ratio
69·9	19·9	11·9	2·5	0·4	2·4	0·9	1·04
55·0	20·5	18·8	3·8	0·6	3·8	1·5	1·00

TABLE 2. *Alkylation of phenol with s-butyl alcohol in sulphuric–acetic acid.*

C_4H_8	PhOH	Na salt	*s*-Butylphenol			2,4-$Bu^s_2C_6H_3$·OH	*ortho*/*para* ratio
76·2	31·4	19·4	4·0	0·4	7·2	0·9	0·56
69·4	25·6	15·5	4·2	0·4	7·7	1·3	0·54

The competitive rearrangement of isopropyl *p*-tolyl ether and *p*-ethylphenyl s-butyl ether was shown to give crossed products; 4-ethyl-2-isopropylphenol and 4-methyl-2,6-di-s-butylphenol were identified by infrared spectroscopy.

Discussion.—Our results show that two of the lines of evidence quoted by Wallis and his collaborators must be rejected. The rearrangement of phenyl s-butyl ether does not give *o*-s-butylphenol as the sole product, and rearrangement of a mixture of two different ethers can give crossed products. There can therefore be little doubt that these rearrangements are at least partly intermolecular.

Comparison of Tables 1 and 2 shows, however, that the products obtained by rearranging phenyl s-butyl ether, and by s-butylating phenol were not identical. A much higher proportion of *ortho*-isomer was obtained in the rearrangement. The rearrangement cannot therefore be entirely intermolecular. A similar conclusion was reached, on similar reasoning, in our previous study of the heterogeneous rearrangements and alkylations catalysed by aluminium chloride; here the conclusion is much more definite since both reactions took place in homogeneous solution under carefully defined conditions. It seems clear that the rearrangement must take place by two distinct paths, one intermolecular, giving predominantly the *para*-isomer, the other giving mainly the *ortho*-isomer.

The work of Gilbert and Wallis [5] suggests very strongly that intermolecular transfer of an s-butyl group from an ether to a phenol takes place with complete loss of configuration. The second reaction must therefore take place with a high degree of retention [3] of configuration, since only part of the product is formed by it, and since the product was 26% resolved. This suggests that the second reaction is indeed an intramolecular rearrangement; it cannot be a bimolecular reaction of phenyl s-butyl ether with phenol or a phenyl ether, since such a reaction would involve partial or complete inversion.

EXPERIMENTAL

Microanalyses were performed by the Microanalytical Laboratory, Imperial College, South Kensington, London, S.W.7, and by Alfred Bernhardt, Max-Planck-Institut, Mülheim, Germany.

Alkyl aryl ethers prepared from the phenol, alkyl bromide, and potassium hydroxide by Niederl and Natelson's method.[2] Isopropyl *p*-tolyl ether had b. p. 197°, n_D^{17} 1·4984; *p*-ethylphenyl s-butyl ether had b. p. 91°/3 mm., n_D^{26} 1·4910; and *p*-ethylphenyl isopropyl ether had b. p. 202°, n_D^{14} 1·4974. See also Part I.

Aryloxyacetic acids were prepared as described earlier [1].

Phenylurethanes were prepared by the procedure of Steinkopf and Hopner [7] and recrystallised from light petroleum (b. p. 60—80°).

p-Ethylphenol, prepared by Clemmensen's method, had m. p. 46°; (aryloxyacetic acid, m. p. 95—96°; phenylurethane, m. p. 121°).

2-*Isopropyl*-4-*methylphenol*.—Bromination of *p*-cresol in carbon tetrachloride at room temperature gave 2-bromo-4-methylphenol, b. p. 77°/2 mm., n_D^{19} 1·5792, which with dimethyl sulphate gave 2-bromo-4-methylanisole, b. p. 84°/1 mm., n_D^{17} 1·5663 (Found: Br, 39·7. Calc. for C_8H_9Br: Br, 39·8%). Acetone (35 g.) in dry ether (100 ml.) was added to a Grignard reagent prepared from magnesium (13·4 g.) and 2-bromo-4-methylanisole (92 g.) in dry ether (200 ml.). After 24 hr. the complex was hydrolysed, the ether layer evaporated, and the residue boiled under reflux for 8 hr. with acetic anhydride (500 ml.), then poured into water. The organic layer was separated and distilled; 2-(2-methoxy-5-methylphenyl)propene (68%) was collected at 57°/0·5 mm. Hydrogenation over 10% palladised charcoal (in ethanol at room temperature and 2 atm.) gave 2-isopropyl-4-methylanisole, b. p. 46°/0·4 mm., n_D^{19} 1·5070 (Found: C, 80·5; H, 9·6. Calc. for $C_{11}H_{16}O$: C, 80·4; H, 9·8%). Demethylation with acetic acid and hydriodic acid gave 2-isopropyl-4-methylphenol,[8] m. p. 35° (Found: C, 80·2; H, 9·4. Calc. for $C_{10}H_{14}O$: C, 80·0; H, 9·4%), (phenylurethane, m. p. 98°; aryloxyacetic acid, m. p. 135°).

4-*Ethyl*-2-*isopropylphenol*.—This was prepared in an analogous manner to the 4-methyl isomer, from 2-bromo-4-ethylanisole, and had b. p. 92°/1 mm., n_D^{20} 1·5562; 2-(5-ethyl-2-methoxyphenyl)propene had b. p. 75°/0·6 mm., n_D^{18} 1·5253; 4-ethyl-2-isopropylanisole had b. p. 218°, n_D^{20} 1·5033; 4-ethyl-2-isopropylphenol had b. p. 227·5°, n_D^{17} 1·5190 (Found: C, 80·4; H, 9·5. Calc. for $C_{11}H_{16}O$: C, 80·5; H, 9·8%) (phenylurethane, m. p. 126°; aryloxyacetic acid, m. p. 95—96°).

4-*Methyl*-2-*s*-*butylphenol*.—This was prepared by a similar method to the isopropylphenols from ethyl methyl ketone. Products were: 2-(2-methoxy-5-methylphenyl)but-2-ene (62%), b. p. 228·5°, n_D^{16} 1·5274 (Found: C, 81·7; H, 9·4. Calc. for $C_{12}H_{17}O$: C, 81·8; H, 9·2%); 4-methyl-2-s-butylanisole, b. p. 72°/0·6 mm., n_D^{19} 1·5049; 4-methyl-2-s-butylphenol, m. p. 43·5—44·5° (Found: C, 80·5; H, 10·0. Calc. for $C_{11}H_{16}O$: C, 80·4; H, 9·8%) (aryloxyacetic acid, m. p. 82°; phenylurethane, m. p. 94—95°).

4-*Ethyl*-2-*s*-*butylphenol*.—This was prepared analogously to the methyl isomer, from ethyl methyl ketone. Products were 2-(5-ethyl-2-methoxyphenyl)but-2-ene, b. p. 245°, n_D^{22} 1·5238; 4-ethyl-2-s-butylanisole, b. p. 72°/0·6 mm., n_D^{18} 1·5025; 4-ethyl-2-s-butylphenol, b. p. 244°, n_D^{19} 1·5152 (Found: C, 80·7; H, 10·2. Calc. for $C_{12}H_{18}O$: C, 80·9; H, 10·2%) (phenylurethane, m. p. 105°).

s-Butylphenols were prepared as described earlier.[1]

4-*Methyl*-2,6-*di*-*s*-*butylphenol*.—But-2-enyl *p*-tolyl ether was prepared and rearranged to 2-but-2′-enyl-4-methylphenol,[9] b. p. 82/0·8 mm., n_D^{19} 1·5259 (phenylurethane, m. p. 63—64°). The butenyl ether, b. p. 88°/0·3 mm., n_D^{17} 1·5220, from this product was boiled under reflux for 5 hr. in dimethylaniline, giving 4-methyl-2,6-bis-(1-methylpropenyl)phenol, b. p. 103°/0·6 mm., n_D^{16} 1·5325. Hydrogenation over palladised charcoal in ethanol gave 4-methyl-2,4-*di*-*s*-*butylphenol*, b. p. 95°/0·5 mm., n_D^{18} 1·5100 (Found: C, 81·5; H, 10·9. $C_{15}H_{24}O$ requires C, 81·8; H, 10·9%) (no solid urethane was obtained).

Rearrangement of Phenyl s-Butyl Ether.—(*a*) Phenyl s-butyl ether (95·5 g.) was heated in sulphuric acid–acetic acid (161 ml.) to 108°; rapid evolution of gas then occurred. The evolved butene was condensed in a cold trap and weighed. After 1·5 hr. the temperature was raised to 120—125° for a further ½ hr.; the mixture became homogeneous and dark red. When cold, the products were partially separated (cf. Wallis *et al.*[3,5]) by addition of 20% ice cold sodium hydroxide solution almost to neutrality and were extracted with ether. The aqueous residue, after several days at 0°, gave a precipitate of sodium hydroxybenzenesulphonate which was dried at 120° (17·5 g.). The hydrocarbon layer was extracted with 4% sodium hydroxide solution. The alkali-soluble material (16·2 g.) was distilled under reduced pressure. Fraction (i) (11·9 g.), b. p. 54—56°/2 mm., gave a phenylurethane, m. p. 128° undepressed on admixture with *ON*-diphenylurethane. Fraction (ii), b. p. 86—90°/2 mm., was shown by infrared spectroscopy to be a mixture of 2- and 4-hydroxyacetophenone. The alkali-insoluble material (6·8 g.) was also

[7] Steinkopf and Hopner, *J. prakt. Chem.*, 1926, **113**, 137.
[8] Carpenter and Easter, *J. Org. Chem.*, 1955, **20**, 401.
[9] Claisen and Tietze, *Ber.*, 1926, **59**, 2344.

distilled. Fraction (*a*), b. p. 72—78°/1 mm., was shown by infrared spectroscopy to be mainly *o*-s-butylphenol with a small amount of phenyl acetate. Fraction (*b*), b. p. 82—88°/1 mm., gave an aryloxyacetic acid, m. p. 112° alone or mixed with *o*-s-butylphenoxyacetic acid. Fraction (*c*), b. p. 92—96°/1 mm., 240°/760 mm., n_D^{20} 1·5110, was shown (infrared) to be a mixture of *o*- (40%), *m*- (9%), and *p*-s-butylphenol (39%). The last fraction, b. p. 100—106°/1 mm., which gave a phenylurethane, m. p. 102° undepressed by *p*-s-butylphenylphenylurethane, was shown (infrared) to contain also 2,4-di-s-butylphenol. s-Butyl acetate (0·2 g.) was recovered from the cold trap protecting the pump.

(*b*) The above rearrangement was repeated with phenyl s-butyl ether (74 g.) and sulphuric acid–acetic acid (125 ml.); the products, separated as above, gave sodium hydroxybenzenesulphonate (21·5 g.), phenol (9·5 g.), and a mixture of hydroxyacetophenones (2·7 g.). The alkali-insoluble fraction (8·3 g.) was analysed spectroscopically.

Alkylation of Phenol by s-Butyl Alcohol.—A sulphuric acid–acetic acid solution (125 ml.) of phenol (46 g., 0·5 mole) and s-butyl alcohol (37 g., 0·5 mole) was heated to 106°, rapid evolution of gas then occurring. The gas was condensed in a cold trap and weighed. The reaction mixture was kept at 106° for 1½ hr. and at 125° for a further ½ hr. The products were partially separated as described above, to give sodium hydroxybenzensulphonate (22 g.), phenol (14·5 g.), and mixed hydroxyacetophenones (4 g.). The material (9·5 g.) insoluble in 4% sodium hydroxide solution was fractionated as before and the various fractions were analysed spectroscopically.

Rearrangement of Mixture of Isopropyl p-*Tolyl Ether and* p-*Ethylphenyl s-Butyl Ether.*—A mixture of isopropyl *p*-tolyl ether (18·2 g., 0·12 mole) and *p*-ethylphenyl s-butyl ether (21·6 g., 0·12 mole) was treated with sulphuric acid–acetic acid (61 ml.) as before. The hydrocarbon layer was extracted with 10% potassium hydroxide solution and then with Claisen solution [potassium hydroxide (350 g.) in water (250 ml.), made up to 1 l. with methanol]. The material (7·5 g.) soluble in potassium hydroxide solution was distilled; fraction (i) (5·1 g.) was shown (infrared) to be a mixture of *p*-cresol and *p*-ethylphenol. The other fraction had an infrared spectrum showing a large carbonyl absorption, indicating that it consisted of acylated phenols. The material (13·3 g.) soluble in Claisen solution was fractionated on a spinning-band column. One fraction was shown (infrared) to be a mixture of 2-isopropyl-4-methylphenol and 4-ethyl-2-isopropyl phenol; another fraction was a mixture of 4-ethyl-2-s-butylphenol and 4-methyl-2,6-di-s-butylphenol. No conclusive results were obtained with the other fractions, which were very complex mixtures.

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820. *Acid-catalysed Rearrangements of Alkyl Aryl Ethers. Part III.*[1] *Rearrangements in the Presence of Aluminium Bromide; the Mechanism of Such Rearrangements.*

By M. J. S. DEWAR and N. A. PUTTNAM.

The rearrangement of phenyl s-butyl ether by a solution of aluminium bromide in chlorobenzene is described. The products are very different from those formed with solid aluminium chloride or sulphuric acid–acetic acid as catalyst. The mechanism of these and some related reactions is discussed and a general mechanism for the acid-catalysed rearrangements of ethers is proposed.

IN the two preceding papers [1] we have given reasons for believing that rearrangement of alkyl aryl ethers to alkylphenols can take place by two routes, one intermolecular and one intramolecular, occurring simultaneously when aluminium chloride or a solution of sulphuric acid in acetic acid is used as catalyst.

[1] Parts I and II, preceding papers.

Two observations in the literature suggested that the intramolecular rearrangement might be favoured if a homogeneous solution of aluminium bromide was used as catalyst. Tarbell and Petropoulos [2] obtained in this way, from benzyl phenyl ether, a mixture of *o*-benzylphenol (55%) and phenol (45%); no *p*-benzylphenol could be detected in the product, even by infrared spectroscopy. The reaction was very fast, being complete in a few seconds at −40°. Tarbell and Petropoulos considered this to be strong evidence for an intramolecular mechanism, since benzylation [3] of phenol by the Friedel–Crafts reaction gives mainly the *para*-isomer, and since rearrangement [4] of benzyl phenyl ether with zinc chloride gave a mixture of *o*- and *p*-benzylphenol.

Hart and Elia [5] found that similar treatment of optically active α-methylbenzyl phenyl ether gave in 22% yield an optically active mixture of α-methylbenzylphenols in which the *ortho*-isomer predominated (85%). Similar rearrangement of optically active α-methylbenzyl *p*-tolyl ether gave 4-methyl-2-(α-methylbenzyl)phenol with 76% retention of configuration, implying an intramolecular mechanism.

This is surprising; for the exceptional stability of benzyl cations would be expected to facilitate an intermolecular mechanism. It seems that aluminium bromide specifically favours intramolecular rearrangements of ethers, and we therefore decided to examine its effect, in chlorobenzene solution, on phenyl s-butyl ether.

The products of this reaction were quite different from those formed [1] with solid aluminium chloride or a solution of sulphuric acid in acetic acid as catalyst. The only alkylphenols obtained were a mixture of the three isomeric mono-s-butylphenols; no dibutylphenols were formed. Moreover, the proportions of the s-butylphenols (Table 1) differed greatly from those observed with other catalysts; this is indicated by the *ortho/para* ratios quoted in Table 2.

TABLE 1. *Products (moles %) obtained by treating phenyl s-butyl ether with aluminium bromide in chlorobenzene.*

			Mono-s-butylphenols		
Time	Temp.	PhOH	*o*-	*m*-	*p*-
10 min.	70—80°	31·8	19·6	Trace	2·5
1 hr.	5—10	33·7	21·8	Trace	1·8
24 hrs.	5—10	32·8	21·8	Trace	2·0

TABLE 2. ortho/para *Ratios of mono-s-butylphenols obtained by rearranging phenyl s-butyl ether with various catalysts.*

Catalyst	$AlCl_3$ (1 mol.)	H_2SO_4–AcOH	$AlBr_3$–PhCl
Temp.	15—20°	110—120°	5—10°
ortho/para Ratio	0·24	1·0	11

Attempts were made to cause s-butyl bromide to react with phenol in the presence of aluminium bromide; after 24 hr. at 5—10° 95% of the phenol was recovered unchanged, together with a small amount (4%) of mixed butylphenols.

Discussion.—Table 1 shows that the proportions of isomers are not much affected by temperature; the differences between the *ortho/para* ratios in Table 2 cannot therefore be due to the different temperatures used in the various reactions. Nor can they be due to steric hindrance, which should be greatest in the case of aluminium bromide. The very high *ortho/para* ratio for the aluminium bromide reaction therefore strongly suggest an

[2] Tarbell and Petropoulos, *J. Amer. Chem. Soc.*, 1952, **74**, 244.
[3] See Thomas, "Anhydrous Aluminium Chloride," Reinhold Publ. Inc., New York, 1941.
[4] Short, *J.*, 1928, 528; Short and Stewart, *J.*, 1929, 553.
[5] Hart and Elia, *J. Amer. Chem. Soc.*, 1954, **76**, 3031.

intramolecular mechanism. This is further supported by the slowness of the reaction between phenol and s-butyl bromide under comparable conditions.

The proportions of isomers formed in the rearrangement of phenyl s-butyl ether, catalysed by aluminium bromide, are moreover very similar to those observed [6] in the acid-catalysed rearrangement of *N*-nitroaniline (*o*, 93; *m*, 0; *p*, 7%; *ortho*/*para* ratio, 13), a reaction which is known [6] to be intramolecular. The intramolecular rearrangement of the ether therefore leads predominantly to the *ortho*-isomer, as postulated in our two previous papers.[1]

In Part II we reviewed the work of Wallis and his collaborators on the rearrangement of optically active phenyl s-butyl ether with a sulphuric acid–acetic acid catalyst; the *o*-s-butylphenol formed had optical activity corresponding to 26% retention of configuration and 74% racemisation. Since Wallis also showed that intermolecular migration of s-butyl leads to complete racemisation, and since intramolecular migration of asymmetric alkyl groups usually takes place with complete retention of configuration, this result suggested that 26% of the rearrangement took place by the intramolecular route, and 74% by the intermolecular route.

Now the proportions of isomers formed by intermolecular migration of an s-butyl group should be the same as those formed by butylation of phenol under the same conditions; these [1] are shown in the first row of Table 3. The second row shows the proportions of isomers formed in the rearrangement catalysed by aluminium bromide (these being the mean of the values given in Table 1). If we assume that the proportions of isomers are the same for intramolecular rearrangements brought about by different catalysts, being those observed for the aluminium bromide reaction, we can calculate the products expected for the rearrangement catalysed by sulphuric acid–acetic acid, the ratio of intermolecular to intramolecular reaction being assumed to be 74 : 26. These values are shown in the third row of Table 3, and the fourth row gives the values observed (Part II). The agreement is within the limits of experimental error and confirms both the dual intermolecular–intramolecular mechanism, and the complete retention of activity in the intramolecular reaction.

TABLE 3. *Proportions of s-butylphenols in various reaction products.*

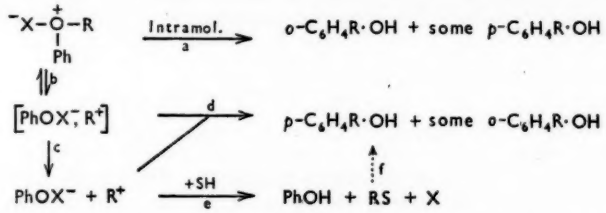
Reaction		$Bu^s \cdot C_6H_4 \cdot OH$ (%) *o*-	*m*-	*p*-
$Bu^sOH + PhOH + H_2SO_4$–AcOH ...		34	4·5	61·5
$Bu^sOPh + AlBr_3$–PhCl		91	—	9
$Bu^sOPh + H_2SO_4$–AcOH	calc.	49	3	48
	obs.	47	7	46

All the available facts can now be rationalised in terms of the annexed mechanism, X being the catalyst (H^+ or aluminium halide) and SH the solvent (if any). Reaction (a) is the intramolecular rearrangement, leading to complete retention of configuration; its mechanism is considered below. Since it involves no fission into ions, it may occur quite readily even under non-polar conditions. Reaction (b) is a reversible fission of the initially formed complex into an ion pair, and (c) is the dissociation of this pair. The ions can recombine (*d*) to form racemic alkylphenols, the *p*-monoalkylphenol predominating, or they can react (*e*) with the solvent to form an alkyl derivative RS which may be able (*f*) to alkylate phenol.

The aluminium bromide reaction. The experimental evidence suggests that this took place almost entirely by the intramolecular route (a); this is not surprising, since the ionisation (b) should be suppressed in the non-polar solvent (chlorobenzene) used, and since any ions that were formed could be removed irreversibly by reaction with the solvent to form alkylchlorobenzenes. In this case reaction (f) cannot occur. Our mechanism

[6] Hughes and Jones, *J.*, 1950, 2678.

implies that rearrangement of optically active phenyl s-butyl ether should take place with complete retention of configuration; this is being investigated.



The sulphuric–acetic acid reaction. Here the reaction appears to take place mainly (74%) by the intermolecular path with complete racemisation, and partly (26%) by the intramolecular path with complete retention of configuration. Acetic acid is a much more polar solvent than chlorobenzene, so the new reaction (b) is faster than reaction (a). In this case reaction of the carbonium ion with the solvent gives an alkyl acetate which can alkylate phenol in presence of the acid catalyst; racemic alkylphenols can be formed by both reactions (d) and (f).

The first product of the ionisation (b) is, however, not an ion pair, but a combination of a cation (R^+) and a neutral molecule (PhOH); the reverse reaction (b) can be largely suppressed by the competing reactions (d) and (e). This means that the original ether is not significantly racemised by reversible ionisation; the intramolecular reaction (a) can therefore give alkylphenols with a very high retention of optical activity.

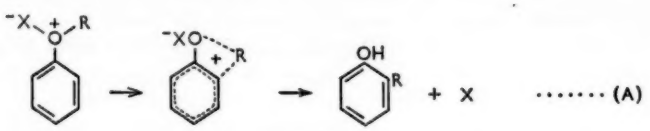
The aluminium chloride reaction. The experimental evidence suggests that (*a*) racemisation is complete, (*b*) most of the reaction is intermolecular, but part takes place by the intramolecular route, (*c*) the proportion of intramolecular reaction is greater, the smaller the amount of catalyst, and (*d*) rearrangement of n-butyl phenyl ether gives the same products as does the s-butyl ether, but in amounts that suggest a greater proportion of intramolecular reaction. It is explained by our reaction scheme if in this case reaction (b) is rapid and reversible, converting the starting material into racemic phenyl s-butyl ether. This would not be surprising; the ionisation (b) should occur very readily on the ionic surface of the catalyst. Observation (c) can be explained if the intramolecular reaction occurs solely in solution, being catalysed by dissolved aluminium chloride whose concentration in solution must be constant (it being present in excess). The rate of the intramolecular reaction should be independent of the amount of catalyst used, whereas the rate of the surface-catalysed intermolecular rearrangement should be proportional to the amount of catalyst. The relative importance of the intramolecular reaction should therefore be greater, the less the total amount of catalyst.

Observation (d) can be explained if aluminium chloride is more soluble in n-butyl phenyl ether than in phenyl s-butyl ether; this seems likely, since co-ordination between the former ether and aluminium chloride should be less sterically hindered.

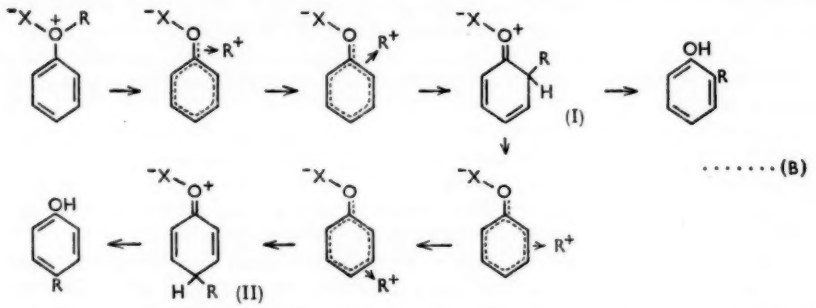
This interpretation can be checked in several ways. First, the optically active phenyl s-butyl ether should racemise faster than it rearranges; secondly, the solubility of aluminium chloride in n- and s-butyl phenyl ether could be measured; thirdly, the reaction could be carried out in solvents in which the solubility of aluminium chloride varied. Experiments along these lines are in progress. It might seem that our mechanism would also require a rapid isomerisation of n-butyl phenyl ether to phenyl s-butyl ether; this, however, is not the case since the s-butyl ether rearranges much more rapidly [1] and would be removed as soon as it was formed. We could detect no isomerisation in a sample of n-butyl phenyl ether after partial rearrangement over aluminium chloride.

Mechanism of the intramolecular rearrangement. The intramolecular acid-catalysed rearrangement of alkyl aryl ethers cannot take place by a classical mechanism, involving

a cyclic transition state, for the latter would contain an impossibly strained four-membered ring (cf. A).

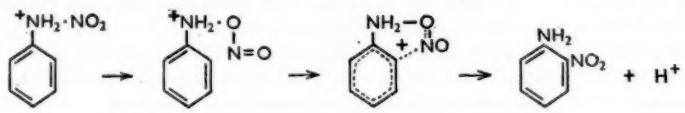


Much the most likely mechanism for this rearrangement, and for the analogous intramolecular acid-catalysed rearrangement of *N*-nitroaniline [6] is the π-complex mechanism suggested by one of us some years ago.[7] Since the problem has recently been reviewed [8] no details need be given here; the proposed mechanism in the present case may be written as in (B). Here (I) is the Wheland intermediate for *ortho*-substitution in



phenol. Since it must be a precursor of the intermediate (II) for *para*-substitution, the rearrangement leads mainly to the *ortho*-isomer. In direct electrophilic substitution of phenol the more favourable intermediate (II) can be formed directly and so *para*-substitution predominates.

The *N*-nitroaniline rearrangement probably takes place in a similar manner. Hughes and James suggested an alternative mechanism in which the nitroaniline first isomerised to phenylhydroxylamine nitrite, which then rearranged *via* a cyclic transition state (III). This mechanism is unacceptable, for two reasons. First, it postulates a reaction which has no analogy and is contrary to the known chemistry of nitramides. If nitramides were to rearrange in presence of acid to hydroxylamine nitrites, they would give rise to products



(III)

which are never observed. Nor can one suppose that the rearrangement is specifically assisted in the case of *N*-nitroaniline by a neighbouring-group participation by phenyl; for such participation would meet the very stereochemical difficulties that the Hughes mechanism was designed to avoid. Secondly, the mechanism does not account for the simultaneous formation of *p*-nitroaniline by a process which, as Hughes and Jones themselves pointed out, must also be intramolecular.

Rearrangements of benzyl phenyl ethers. The extraordinary facility [2,5] with which

[7] Dewar, *J.*, 1946, 406; "The Electronic Theory of Organic Chemistry," Oxford, 1949.
[8] Dewar, "Theoretical Organic Chemistry (Kekulé Symposium)," Butterworths, London, 1959.

benzyl phenyl ethers rearrange in presence of aluminium bromide suggests that these reactions may differ from the corresponding rearrangements of alkyl aryl ethers. There is a formal similarity [8] between the rearrangement of benzyl phenyl ether to *o*-benzylphenol, and that of a hydrazobenzene derivative to an *o*-semidine. This is being investigated.

Experimental

For general directions see Parts I and II.[1]

o-*s-Butylphenol.*—A solution of but-2-enyl phenyl ether, b. p. 55°/0·5 mm., n_D^{19} 1·5210 (9·5 g.), in diethylaniline (60 ml.) was boiled under reflux for 4 hr. When cold, the solution was poured into hydrochloric acid and extracted with light petroleum (b. p. 40—60°). The hydrocarbon layer was extracted with Claisen solution [potassium hydroxide (350 g.) in water (250 ml.) made up to 1 l. with methanol]; acidification and distillation gave *o*-1-methylallylphenol, b. p. 76°/2 mm., n_D^{21} 1·5382 (phenylurethane, m. p. 88—89°). Hydrogenation over 10% palladised charcoal in ethanol gave *o*-s-butylphenol which was shown by infrared spectroscopy to be identical with that synthesised earlier.[1]

Aluminium Bromide Solution.—A solution of anhydrous aluminium bromide in chlorobenzene was prepared, filtered, and stored under nitrogen in absence of moisture; 1 g. of solution contained 0·19 g. of the bromide.

Rearrangement of Phenyl s-Butyl Ether.—(a) *At* 70°. Aluminium bromide solution (157·4 g., 0·11 mole of aluminium bromide) was added with stirring to a solution of phenyl s-butyl ether (16·5 g., 0·11 mole) in chlorobenzene (20 g.). The mixture became hot (70°) and hydrogen bromide was evolved. After 10 min. the reaction was stopped by addition of water (500 ml.). The organic layer was taken up in light petroleum (b. p. 40—60°) and extracted with Claisen solution. Acidification gave a phenolic product (7 g.) which were fractionated in a 15 ml. "Towers" semimicro-apparatus. Fraction (i) (3 g.), b. p. 50—6°/1·5 mm., gave a phenylurethane, m. p. 126·5° alone or mixed with *ON*-diphenylurethane. Fraction (ii) was shown (infrared) to be a mixture of phenol and *o*-s-butylphenol. Fraction (iii), b. p. 78—80°/1 mm., gave a phenylurethane, m. p. 85°, alone or mixed with *o*-s-butylphenyl phenylurethane (corresponding aryloxyacetic acid, m. p. and mixed m. p. 112°). The last fraction was shown (infrared) to be mainly *o*-s-butylphenol with some *p*-s-butylphenol and traces of the *meta*-isomer.

(b) *At* 5—10°. The rearrangement was repeated with excess of chlorobenzene (300 ml.), the temperature was kept at 5—10°. After 1 hr. the phenolic products (7·5 g.) were separated as above and analysed by infrared spectroscopy.

(c) *At* 5—10° *for* 24 *hr.* Experiment (b) was repeated but the mixture was stirred for 24 hr. before addition of water. The phenolic products (7·4 g.), separated in the usual manner, were analysed spectroscopically.

Alkylation of Phenol by s-Butyl Chloride.—(*a*) Aluminium bromide solution (79 g., 0·055 mole) was added to mixture of phenol (5·2 g., 0·055 mole) and s-butyl bromide (7·5 g., 0·055 mole) in chlorobenzene (150 ml.) as described in (b) above. The reaction was stopped after 1 hr.; the phenolic products (4·9 g.) were shown (infrared) to be phenol with a very small amount of s-butylphenols. (*b*) The alkylation was repeated, but allowed to occur for 24 hr. before addition of water. The phenolic material was shown to be phenol with 4—5% of s-butylphenols.

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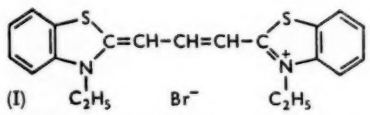
821. *The Crystallography of Some Cyanine Dyes. Part II.*[1] *The Molecular and Crystal Structure of the Ethanol Solvate of 3,3′-Diethylthiacarbocyanine Bromide.*

By P. J. Wheatley.

The structure of the 1 : 1 solvate of ethanol and 3,3′-diethylthiacarbocyanine bromide has been determined by *X*-ray single-crystal methods from two projections. The conjugated chain is in the extended form with the sulphur atoms *cis* with respect to this chain. The methyl groups of the ethyl substituents lie on opposite sides of the cationic plane. The cation is not quite planar, the two halves being twisted through an angle of 8°.

In Part I the *X*-ray analysis of unsolvated crystals of 3,3′-diethylthiacarbocyanine bromide (I) was described. The solvated crystals used for the present work exhibited the same increase in internal disorder with time as the unsolvated crystals, and to about the same extent. However, the solvated crystals appear to be indefinitely resistant to spontaneous disintegration.

Structure Determination.—$C_{23}H_{27}N_2OS_2Br$, $M = 491{\cdot}5$, triclinic, $a = 8{\cdot}07_2 \pm 0{\cdot}05$, $b = 11{\cdot}82_8 \pm 0{\cdot}08$, $c = 13{\cdot}10_5 \pm 0{\cdot}08$ Å, $\alpha = 98°\ 45'$, $\beta = 77°\ 14'$, $\gamma = 103°\ 17'$, $U = 1181$ Å^3, $D_m = 1{\cdot}42$ (by flotation), $Z = 2$, $D_c = 1{\cdot}382$, $F(000) = 508$. Space group, $P\bar{1}$ (C^1_i, No. 2). Cu-K_α radiation ($\lambda = 1{\cdot}542$ Å), single-crystal rotation and Weissenberg photographs.



The crystals, which were needles elongated parallel to the short [*a*] axis, showed a considerable spread in the measured density, and the value of D_m obtained by flotation was not accurate enough to decide whether there were one or two molecules of ethanol in the asymmetric unit. The crystal analysis showed, however, that the crystals were actually a 1 : 1 solvate.

Multiple-film Weissenberg photographs round [*a*] were obtained with an approximately square needle about 0·13 mm. across. The *hk*0 photographs were obtained from a cube of side 0·1 mm. cut from a needles. No correction was made for absorption ($\mu = 44{\cdot}0$ cm.$^{-1}$). Relative intensities were estimated by comparison with standard strips prepared from the same crystals. 212 of the 339 0*kl* reflexions, and 156 of the 328 *hk*0 reflexions obtainable with Cu-K_α radiation were observed to be non-zero.

The 0*kl* projection was solved first. A Patterson synthesis gave the co-ordinates of the bromide ion. The phases determined from these co-ordinates were used for a preliminary Fourier synthesis. On the resultant electron-density map the peaks due to the two sulphur atoms could be identified. The phases determined from these three heavy atoms were used to compute a second Fourier synthesis which could readily be interpreted in terms of all the atoms including those of one ethanol molecule. The projection was refined by Fourier and difference syntheses until *R* had fallen to 14%. Unobserved reflexions were omitted from the *R* factors. A single isotropic temperature factor, $B = 4{\cdot}75$ Å^2, was used. At this stage it appeared that the crystal structure was basically very similar to that of the unsolvated crystals, and that the stereochemistry of the cation was practically identical. It was noticed that the model of the cation used for the unsolvated crystals did not fit particularly well over the peaks in this projection

[1] The paper, *J.*, 1959, 3245, is considered as Part I, of this series.

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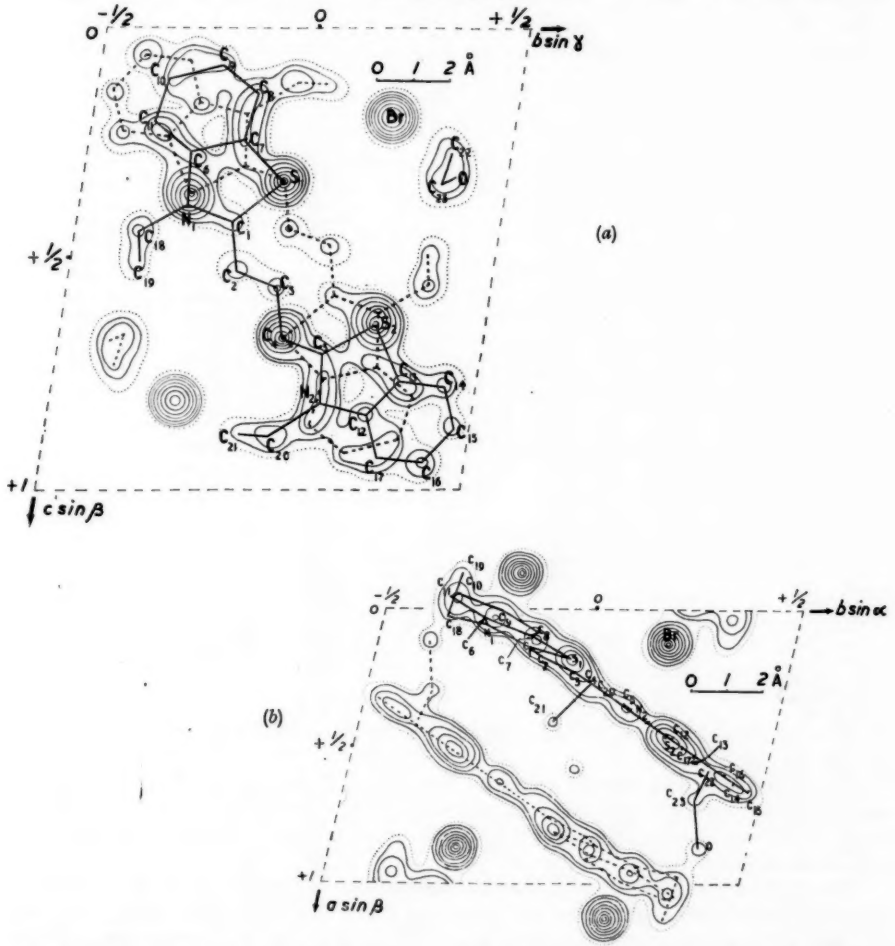
of the solvated crystals, but this was attributed to insufficient refinement in the poorly resolved projection.

The solution of the *hk*0 projection was attempted in the same way, but offered some difficulties until it was realized that, in an unsharpened Patterson synthesis, no Br–Br or

FIG. 1. (*a*) *Projection of the contents of the unit cell down* [*a*]. (*b*) *Projection of the contents of the unit cell down* [*c*].



The contours are drawn at 50, 100, 200 . . . arbitrary units, except in the bromine peaks where some contours have been omitted.

Br–S peaks could be seen. Only in a sharpened Patterson synthesis did these peaks involving the three heavy atoms appear. Moreover, the two strongest reflexions ($\bar{2}20$ and $\bar{4}40$ with unitary structure factors of 0·57 and 0·56 respectively) had phases opposite to that of the bromine atom. Once these difficulties had been overcome, refinement proceeded by Fourier methods until R had dropped to 24%. At this stage it had already been decided that the methyl groups of the ethyl substituents must lie on opposite sides of the cationic plane, whereas in the unsolvated crystals the methyl groups lie on the same

side. However, despite many trials, no positions were found for the atoms of a planar cation that would reduce R below 24%. Reluctantly, the notion of a planar cation had to be abandoned, and, as soon as the two halves of the cation were assumed to be twisted out of co-planarity, R began to drop again. The model that gave the best agreement with the observed intensities was one in which one half of the cation was viewed exactly sideways on, and the twist occurred about the bond of C(2)–C(3) of the conjugated chain. However, although this projection is suitable for deciding whether or not the cation is planar, the lack of resolution makes it difficult to decide exactly how the departure from planarity is achieved. A three-dimensional analysis is really needed to establish whether

TABLE 1. *Fractional co-ordinates* (x/a, y/b, z/c) *and orthogonal co-ordinates* (X, Y, *and* Z *in* Å).

Atom	x/a	y/b	z/c	X	Y	Z
Br	0·129	0·202	0·190	1·489	1·771	2·415
$S_{(1)}$	0·193	−0·030	0·330	2·343	−1·371	4·194
$S_{(2)}$	0·470	0·211	0·639	5·293	0·705	8·120
O	0·875	0·376	0·320	7·676	2·186	4·067
$N_{(1)}$	0·062	−0·247	0·372	1·418	−3·779	4·727
$N_{(2)}$	0·373	0·138	0·812	4·964	−0·679	10·319
$C_{(1)}$	0·140	−0·137	0·421	2·154	−2·719	5·350
$C_{(2)}$	0·178	−0·123	0·523	2·709	−2·828	6·646
$C_{(3)}$	0·242	−0·005	0·562	3·309	−1·628	7·142
$C_{(4)}$	0·260	0·008	0·668	3·716	−1·719	8·489
$C_{(5)}$	0·363	0·117	0·707	4·623	−0·699	8·984
$C_{(6)}$	0·030	−0·250	0·270	0·912	−3·551	3·431
$C_{(7)}$	0·100	−0·136	0·241	1·389	−2·275	3·062
$C_{(8)}$	0·090	−0·122	0·139	1·055	−1·887	1·767
$C_{(9)}$	0·010	−0·217	0·078	0·274	−2·741	0·991
$C_{(10)}$	−0·058	−0·329	0·111	−0·177	−4·006	1·411
$C_{(11)}$	−0·050	−0·348	0·213	0·140	−4·448	2·706
$C_{(12)}$	0·482	0·244	0·842	5·896	0·313	10·700
$C_{(13)}$	0·543	0·311	0·755	6·157	1·167	9·594
$C_{(14)}$	0·643	0·422	0·769	6·977	2·265	9·773
$C_{(15)}$	0·680	0·472	0·867	7·514	2·593	11·018
$C_{(16)}$	0·618	0·405	0·953	7·242	1·744	12·111
$C_{(17)}$	0·510	0·293	0·938	6·356	0·650	11·920
$C_{(18)}$	0·033	−0·352	0·428	1·331	−5·077	5·439
$C_{(19)}$	−0·133	−0·342	0·507	0·225	−4·809	6·443
$C_{(20)}$	0·273	0·045	0·880	4·349	−1·729	11·183
$C_{(21)}$	0·420	−0·020	0·875	5·491	−2·760	11·120
$C_{(22)}$	0·588	0·358	0·265	5·283	2·615	3·368
$C_{(23)}$	0·695	0·342	0·342	6·317	2·074	4·346

all the twisting occurs about the C(2)–C(3) bond, or whether small twists about other bonds are also playing a part.

The final R factor for the $hk0$ projection was 17%. It was not necessary to introduce anisotropic temperature factors as in the unsolvated crystal, an overall temperature factor of 5·12 Å^2 being sufficient to obtain satisfactory agreement between the calculated and observed intensities.

The scattering factors used in this analysis were those of Berghuis *et al.*[2] for the carbon, nitrogen, and oxygen atoms; that of Tomiie and Stam [3] for the sulphur atom; and that of Thomas and Umeda [4] for the bromide ion. Thomas and Umeda's figures were modified at low values of θ for the additional electron, and corrected for the real part of the dispersion.[5] The deficiency of one electron spread out over many atoms of the cation was ignored.

Electron-density maps projected down [a] and [c] are shown in Figs. 1 (a) and (b), respectively. The molecule drawn in full lines corresponds to the co-ordinates listed in Table 1. Apart from the fractional co-ordinates with respect to the original triclinic axes,

[2] Berghuis, Haanappel, Potters, Loopstra, MacGillavry, and Veenendaal, *Acta Cryst.*, 1955, **8**, 478.
[3] Tomiie and Stam, *ibid.*, 1958, **11**, 126.
[4] Thomas and Umeda, *J. Chem. Phys.*, 1957, **26**, 293.
[5] Dauben and Templeton, *Acta Cryst.*, 1955, **8**, 841.

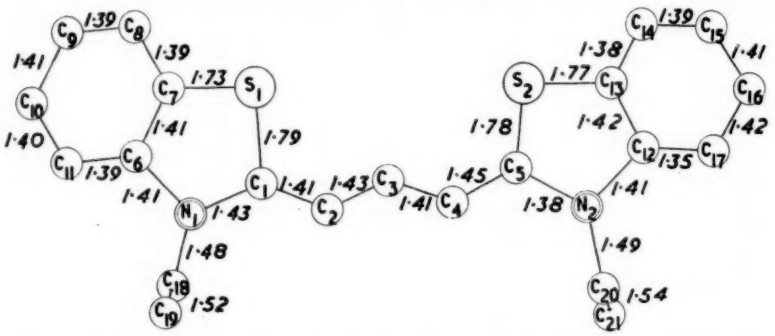
TABLE 2. *Observed and calculated structure factors for one asymmetric unit.*

hkl	F_o	F_c	*hkl*	F_o	F_c	*hkl*	F_o	F_c	*hkl*	F_o	F_c	*hkl*	F_o	F_c
0.0.1	3·8	−3·7	1	9·4	−11·0	12	4·4	−5·7	12	3·0	−3·3	5	11·5	−12·0
2	54·2	−53·8	3	6·7	+7·6	13	5·5	−3·7	13	3·3	−3·0	6	23·5	+20·8
3	14·7	−14·6	4	9·3	+10·7	14	2·7	+3·8	1.0.0	21·8	+23·2	7	11·7	−9·9
4	15·9	−18·1	5	3·0	−3·8	15	5·0	+4·0	1	5·3	+7·4	8	15·9	−15·0
5	4·8	+6·8	6	11·5	−13·5	0.$\bar{5}$.1	13·5	−12·8	2	35·2	−33·8	9	5·8	−7·0
6	19·5	+18·9	0.8.2	6·0	+2·6	2	6·0	+3·2	3	12·5	+15·7	10	1·8	+1·5
7	16·7	−15·7	3	4·8	+4·0	3	7·6	−7·8	4	4·7	+4·7	11	3·3	+2·4
8	12·5	−10·0	5	5·2	−6·1	4	28·7	−26·4	5	20·9	+13·9	12	2·2	−4·0
9	5·9	+4·6	7	7·2	+10·6	5	32·2	+29·0	6	2·3	+2·3	13	5·2	−5·7
11	4·4	+3·1				6	10·3	+11·7	7	15·7	−13·8	$\bar{2}$.1.0	10·6	−12·3
13	8·2	−7·9	0.9.0	9·5	+13·2	7	13·7	−13·0	8	4·1	+4·6	2	91·0	−83·3
0.1.0	32·2	+31·1	1	13·7	+13·7	8	7·5	−8·9	9	12·7	+12·5	3	20·4	−14·6
1	20·1	+17·4	3	5·9	−5·5	9	5·6	−6·5	10	5·3	+4·3	4	13·7	−14·2
2	22·0	−22·0	4	4·7	−8·3	10	7·1	+7·2	12	3·6	−3·7	5	6·6	−7·5
3	24·5	+21·7	5	4·0	−7·2	11	10·2	+7·6	14	1·9	+2·4	6	2·4	+6·7
4	8·9	+7·4	6	3·1	+7·3	13	6·6	−5·0	2.0.0	19·2	+19·0	7	11·4	+9·8
5	3·3	+4·3	7	3·6	+3·1	0.$\bar{5}$.1	17·8	+20·1	1	26·9	−32·0	8	5·5	−8·0
6	11·0	+11·3	0.10.1	10·6	+14·5	2	17·1	+16·7	2	22·9	−22·2	9	16·7	−14·9
7	18·7	−18·7	3	5·3	−7·3	3	25·2	−24·3	3	11·3	+11·7	10	8·8	−6·6
8	9·4	−6·8	4	4·2	+7·6	4	18·3	−15·2	4	23·8	+18·8	12	5·9	+5·5
9	18·6	+18·1	8	4·5	−7·1	6	6·4	+7·4	5	4·7	−4·7	14	2·5	−3·0
10	6·8	+5·1	0.11.0	4·4	−4·3	7	8·2	+7·7	6	22·3	−24·7	$\bar{3}$.1.0	14·9	−11·4
11	4·9	−4·8	1	4·2	−6·2	12	6·6	+6·8	7	17·0	−18·2	2	28·3	+27·3
13	7·3	− 6·6	4	6·4	+9·1	14	4·7	−4·0	8	14·3	+13·2	3	13·7	−10·0
15	4·7	+4·2				0.$\bar{7}$.1	6·7	+6·0	9	17·0	+15·3	4	23·7	−23·8
			0.12.0	3·0	−3·7	2	9·8	+9·6	11	4·4	−3·2	5	11·4	−11·7
0.2.0	39·9	−39·3	1	3·7	−6·3	3	8·0	+7·2	13	1·5	+1·9	6	7·6	+7·4
2	11·4	−10·3				4	6·5	−6·6	3.0.0	21·7	−22·9	7	10·4	+12·2
3	10·5	+12·5	0.$\bar{1}$.1	32·0	−37·2	5	10·6	−10·1	1	25·2	−26·5	8	5·0	−6·6
4	20·3	+20·9	2	4·6	+2·5	7	6·8	+6·6	2	8·0	+6·7	9	2·3	−5·5
5	40·2	−36·9	3	33·8	−31·3	8	9·2	+8·2	3	18·7	+16·9	10	3·0	−1·9
6	12·5	−15·5	4	48·2	−37·3	10	13·7	−13·9	4	1·8	−4·3	11	1·8	+2·9
7	8·6	+12·8	5	9·6	−6·3	11	3·9	−4·2	5	9·6	−11·4	12	5·0	+5·4
8	5·5	+5·1	6	15·7	+14·6	12	6·3	+5·4	6	6·7	−7·7	$\bar{4}$.1.0	14·3	−6·8
9	15·1	+16·2	7	21·1	+22·7				8	7·4	+6·9	3	42·6	+36·5
11	14·8	−16·8	8	8·2	−9·3	0.$\bar{8}$.1	18·4	−22·6	9	2·8	+1·6	4	41·7	+33·9
0.3.0	9·5	+11·3	9	7·9	−9·0	3	16·3	+19·0	10	2·5	−3·8	5	9·2	−14·0
1	6·0	−6·0	11	7·7	+8·4	5	4·4	−5·1				7	13·9	+15·2
2	34·1	+34·8	12	6·0	+5·0	6	5·1	−5·4	4.0.0	14·5	−15·2	8	13·9	+13·4
3	13·6	+17·1	14	6·1	−6·1	7	6·5	−6·4	1	2·5	+5·7	10	2·4	−4·0
4	17·2	−22·3				8	8·3	+7·7	2	2·0	+4·2	11	3·6	+4·0
5	23·7	−22·9	0.$\bar{2}$.1	12·7	−13·4	9	5·3	+4·5	3	6·7	+6·6	12	6·7	+7·7
6	2·8	−1·6	2	49·8	+46·9	10	5·7	−5·3	5	7·6	−4·1	13	2·6	+3·3
7	9·8	+12·1	3	16·2	+18·3	13	3·2	−2·0	6	6·9	−5·8			
8	6·9	+7·2	4	24·1	−26·7	14	6·7	+5·3	7	5·5	−3·5	$\bar{5}$.1.0	4·4	−3·3
11	4·9	−5·0	5	18·0	−15·4				10	6·4	−5·2	2	4·2	+8·0
			6	6·1	+11·2	0.$\bar{5}$.1	18·5	−19·1	12	1·8	+1·6	3	17·6	+17·6
0.4.0	10·9	+11·0	7	19·9	+20·3	2	4·7	−2·4				5	4·2	+4·2
1	22·8	+25·2	8	3·3	+0·9	4	8·2	+7·3	5.0.0	6·9	−8·4	7	2·7	+1·9
2	5·8	+7·6	9	12·5	+10·0	5	14·5	+13·8	1	5·0	+10·4	9	4·7	+4·1
3	6·4	+0·9	10	7·9	−7·3	6	5·4	−4·5	2	19·0	+19·7	11	3·8	−4·4
4	32·3	−33·8	11	11·4	−9·4	7	11·0	−9·4	3	1·7	+0·9			
5	6·2	−2·6	12	4·9	+4·5	9	3·6	±4·2	4	7·6	−6·1	$\bar{6}$.1.0	9·3	−12·8
6	13·6	+15·3	14	3·5	−2·6	12	5·8	−4·5	5	3·8	−2·8	2	7·1	−10·2
7	7·3	+4·3							6	2·4	+3·3	3	10·2	+5·6
8	4·9	−2·9	0.$\bar{3}$.1	32·7	−29·7	0.10.3	4·4	−5·8	7	3·1	+6·2	4	11·1	+11·5
9	6·6	−9·1	2	11·5	−16·3	5	6·7	+6·8	9	3·9	−4·1	5	17·5	−12·5
11	5·6	+7·7	3	47·7	+48·4	8	4·3	−5·8	10	1·9	−0·9	6	17·2	−17·6
12	4·2	+3·2	4	16·3	+17·2	9	3·2	−1·3				7	3·0	−3·5
			5	30·5	−29·9	11	3·4	+2·9	6.0.0	8·7	+4·3	12	2·4	−2·9
0.5.0	23·7	+26·8	6	7·5	−7·1				1	8·6	+9·2	13	2·2	−1·1
1	16·4	+18·1	7	9·3	−9·2	0.$\bar{11}$.1	4·9	+5·3	3	7·0	−10·5			
2	25·7	−32·4	8	5·7	+5·3	2	3·7	+3·2	4	2·4	−3·9	7.1.0	2·1	−2·2
4	13·1	+13·4	9	28·0	+24·1	3	4·2	−2·7	5	9·2	+7·9	2	3·3	−7·2
6	13·9	+12·9	10	14·6	−14·8	4	5·0	−7·5	6	7·9	+6·6	3	2·4	−3·1
7	2·9	−4·9	11	12·2	−12·0	6	4·3	+5·3				5	2·3	+2·3
8	15·8	−17·7	15	4·3	+2·4	10	5·1	−1·8	7.1.0	1·8	+2·3	6	2·3	+1·0
9	3·7	+9·6							5	2·9	+4·0	7	9·2	−12·3
			0.$\bar{4}$.1	17·7	−20·4	0.$\bar{12}$.2	3·7	+6·2	6	2·2	+3·3	8	3·9	−3·1
0.6.0	4·4	+9·2	2	19·6	−18·2				8.2.0	1·6	−4·1	11	1·8	−1·6
1	18·8	−21·1	3	22·3	+20·1	0.1.0	32·2	+31·0	3	5·5	−5·5	12	1·8	−3·3
2	23·8	−19·9	4	13·1	−11·7	2	39·9	−39·2	5	3·0	+3·4			
4	21·3	+19·7	5	10·2	+10·8	3	9·5	+11·2				$\bar{8}$.2.0	4·5	−4·3
6	5·0	−3·5	6	4·7	+2·9	4	10·9	+10·9	9.1.0	2·5	−3·4	3	1·4	−2·7
8	9·1	−9·7	7	21·4	−19·9	5	23·7	+26·3	2	2·9	−3·1	5	1·7	+3·6
9	9·2	+11·3	8	3·2	+4·0	6	4·4	+9·0				7	4·8	+1·9
10	4·4	+6·0	9	14·8	+13·1	7	9·2	−8·6	$\bar{1}$.1.0	15·7	+17·7			
11	3·4	−4·8	10	4·8	−3·1	9	9·5	+12·5	3	41·1	−42·0	$\bar{9}$.2.0	1·4	+2·1
0.7.0	9·1	−8·9	11	4·9	+3·2	11	4·4	−3·9	4	33·8	−24·7	3	2·0	−3·4

there are also given in Table 1 the co-ordinates in Å with respect to orthogonal axes. These orthogonal axes are oriented as follows: $[b_0]$ coincides with the original triclinic axis $[b]$; $[a_0]$ is the projection of the triclinic axis $[a]$ on to the plane perpendicular to $[b_0]$; $[c_0]$ is perpendicular to $[a_0]$ and $[b_0]$. The following relations then hold: $X = x \sin\gamma + z(\cos\beta - \cos\alpha\cos\gamma)/\sin\gamma$; $Y = y + x\cos\gamma + z\cos\alpha$; $Z = z[\sin^2\alpha - \{(\cos\beta - \cos\alpha\cos\gamma)/\sin\gamma\}^2]^{\frac{1}{2}}$. The lengths of the orthogonal axes are $a_0 = 7{\cdot}85_6$, $b_0 = 11{\cdot}82_8$, $c_0 = 12{\cdot}70_8$ Å. The molecular dimensions and the numbering of the atoms are shown in Fig. 2.

Results.—The analysis shows that, apart from the methyl groups of the ethyl substituents, the remaining atoms of the cation no longer lie in one plane as they do in the same cation in the unsolvated crystals, but that the atoms lie in two planes making an angle of about 8° with each other. The methyl groups lie on opposite sides of the cation. Apart from these differences the crystal structures of the solvated and unsolvated crystals are very similar. Columns of cations, each pair being centrosymmetrically related, are stacked parallel to the [*a*] axis. The bromide ions and ethanol molecules lie between these columns.

FIG. 2. *The numbering of the atoms, and the molecular dimensions.*



The molecular dimensions shown in Fig. 2 are close to the expected values and to the values obtained in Part I. The distances C(22)–C(23) and C(23)–O in the ethanol molecule are 1·52 and 1·39 Å respectively. The intermolecular contacts are normal, with the exception of the Br . . . O distance which is only 3·27 Å, indicating, perhaps, the presence of a weak hydrogen bond between the bromine ion and the oxygen atom. The only other bromine contacts of less than 3·8 Å are S(1) at 3·71 Å and C(8) at 3·74 Å. There appear to be no short contacts between the ethanol molecule and the atoms of the cation that might account, in terms of packing forces, for the departure of the cation from planarity.

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822. *Peptides. Part IX.* Preparation of* L-*Phenylalanine from* L-*Tyrosine.*

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Reduction by sodium in liquid ammonia of the diethyl phosphate of L-tyrosine, prepared through the cupric salt, gives L-phenylalanine, conveniently isolated as its *N*-acetyl derivative which may be converted directly by ethanolic hydrogen chloride into the ethyl ester of L-phenylalanine hydrochloride.

IN studies of synthetic peptides L-phenylalanine finds frequent application but it is expensive. In contrast, its near relative, L-tyrosine, is readily available from casein and other natural proteins, and the current retail prices of the two amino-acids are in a ratio of 35 : 1. Consequently, when we discovered an efficient method of reducing phenols to

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aromatic hydrocarbons,[1] L-tyrosine was an obvious subject for it.* The complications introduced by the presence of the amino- and carboxyl groups have now been mastered, and we are able to describe a preparative method which gives consistently a 42% over-all conversion of L-tyrosine into L-phenylalanine.

Our general reductive method is based on the reaction between the aryl diethyl phosphate and sodium in liquid ammonia, and hence the phenylalanine must be separated from alkali-metal salts. On a preparative scale, it is most convenient to extract the amino-acid as its *N*-acetyl derivative, from which it can be regenerated in excellent yield; moreover, after acetylation, the contaminating tyrosine, which is an inevitable by-product of the reduction,[1] can be destroyed by permanganate. If the ethyl ester of phenylalanine is required, its hydrochloride can be prepared directly from *N*-acetylphenylalanine. Alcoholysis has not apparently been combined with esterification before in just this way, but the process may be generally useful with α-acetamido-acids. Unfortunately, it fails with benzyl alcohol.

$$ArO{\cdot}PO(OEt)_2 \xrightarrow[NH_3]{Na-} ArH$$

The phenolic hydroxyl group of L-tyrosine can be phosphorylated cleanly in aqueous alkali with tetraethyl pyrophosphate when the amino- and the carboxyl group are masked in the cupric salt, just as in the familiar ω-acylation of αω-diamino-carboxylic acids.[3] Provided that the cupric ions are removed carefully with hydrogen sulphide, the reduction is smooth and 43% of the tyrosine is converted into *N*-acetyl-L-phenylalanine. It is noteworthy that, as judged by the small consumption of permanganate, only a little tyrosine is regenerated during the reduction; most of the losses probably occur before this stage.

An alternative way, which attracted us, of masking the amino-group is to acetylate it before phosphorylation of the phenolic hydroxyl group, instead of after the reduction. The methyl ester of *N*-acetyl-L-tyrosine, a very accessible intermediate, gives a nicely crystalline diethyl phosphate, which however is converted by sodium in liquid ammonia into a complex mixture. Reduction of the analogous benzyl ester is much more satisfactory, presumably because the carboxyl group is liberated quickly, but the process is not competitive. On the other hand these difficulties do not arise with *N*-acetyl-L-tyrosine itself and, since this intermediate need not be isolated before phosphorylation and the over-all yield is almost as good, this route would be preferable to that *via* the cupric salts, were it not for a small amount of racemisation which is apparently unavoidable. Racemisation can occur easily during the acetylation of α-amino-acids but it is avoided when the solution is alkaline;[4] we confirmed that the stage of acetylation was not responsible in the present instance by comparing the *N*-acetyl-L-tyrosine with a sample prepared from the benzyl ester by hydrogenolysis. Clearly, the mixed anhydrides of *N*-acetyl-L-tyrosine and its diethyl phosphate with diethyl hydrogen phosphate are responsible, because they can have transient existence during the treatment with tetraethyl pyrophosphate. In this connection we were able to show, by means of a Carlsberg recording titrator (" pH-stat "),[5] that acetate ions accelerate the alkaline hydrolysis of tetraethyl pyrophosphate, presumably through formation of acetyl diethyl phosphate.

As racemisation is not usually encountered with α-toluene-*p*-sulphonamido-acids and they are cleaved by sodium in liquid ammonia,[6] we prepared the crystalline diethyl phosphate of *N*-toluene-*p*-sulphonyl-L-tyrosine, but this route is inconvenient. A rather

* The method has also been used elsewhere.[2]

[1] Kenner and Williams, *J.*, 1955, 522.
[2] Pelletier and Locke, *J. Amer. Chem. Soc.*, 1957, **79**, 4531; *J. Org. Chem.*, 1958, **23**, 131; Wenkert and Jackson, *J. Amer. Chem. Soc.*, 1958, **80**, 217.
[3] Goodman and Kenner, *Adv. Protein Chem.*, 1957, **12**, 508.
[4] Neuberger, *Adv. Protein Chem.*, 1948, **4**, 357.
[5] Jacobsen, Léonis, Linderstrøm-Lang, and Ottesen, " Methods of Biochemical Analysis " (ed. D. Glick), Interscience Publishers, New York, Vol. IV, 1957, p. 171.
[6] Du Vigneaud and Behrens, *J. Biol. Chem.*, 1937, **117**, 27.

similar, but more direct, route begins with reaction between L-tyrosine itself and tetraethyl pyrophosphate, but in this instance the reduction gives a complex mixture, apparently containing peptides, and the over-all yield is only 8%.

Experimental

Paper chromatograms were run on Whatman No. 1 paper in the system butan-1-ol–acetic acid–water (4 : 1 : 5 v/v).

Tetraethyl Pyrophosphate.—When commercial material was not available, the following procedure [7] was convenient. A mixture of diethyl phosphite (51 c.c.), carbon tetrachloride (71·2 c.c.), and ether (200 c.c.) was stirred at 0° during the dropwise addition of triethylamine (27·8 c.c.) and then for a further hour before addition of triethylamine (second portion of 27·8 c.c.) and water (6·5 c.c.). The mixture was kept overnight at 5° and then filtered. The triethylamine hydrochloride was washed with ether. Vacuum-distillation of the combined liquors afforded 41·5 g., b. p. 126—128°/0·4 mm., n_D^{22} 1·4170.

N-*Acetyl*-L-*Phenylalanine.*—A solution of hydrated cupric sulphate (12·43 g.) in hot water (20 c.c.) was added gradually to a stirred solution of L-tyrosine (18·1 g.) in hot 2N-sodium hydroxide (50 c.c.). The mixture was cooled to room temperature and the cupric salt was dissolved by the addition of 2N-sodium hydroxide (50 c.c.) and water (80 c.c.). Tetraethyl pyrophosphate (40 g.) was added in one portion to this solution (pH 11·0), and then the pH was maintained at 11·0 by dropwise addition of 2N-sodium hydroxide (55 c.c.) with rapid stirring. The pH was reduced to 7·0 with hydrochloric acid. The light blue precipitate was collected, washed with water (100 c.c.), and dissolved in 4N-hydrochloric acid. Hydrogen sulphide was bubbled through the solution until precipitation of cupric sulphide was complete and then the filtered liquor was neutralised (pH 7·0) and evaporated under reduced pressure. The residual solid was dried by azeotropic distillation with benzene and dissolved in liquid ammonia (100 c.c.) before being added rapidly to a solution of sodium (9·2 g.) in liquid ammonia (50 c.c.). The remaining blue colour was discharged with ammonium chloride, and the ammonia was allowed to evaporate. A solution of the residue in water (100 c.c.) was made alkaline, boiled to remove the last of the ammonia, cooled, and then brought to pH 11·0. Acetic anhydride (24 c.c.) and 2N-sodium hydroxide (240 c.c.) were added in eight equal portions to the solution which was stirred at 0°. After being allowed to reach room temperature during 1 hr., the solution was acidified and extracted with ethyl acetate (10 × 50 c.c.). When the bulk of the ethyl acetate (450 c.c.) had been distilled, most (8·0 g.) of the product crystallised. The liquors were extracted with aqueous sodium carbonate solution, to which potassium permanganate solution was added until the colour persisted for 10 min. It was discharged with sodium sulphite and then extraction of the acidified solution with ethyl acetate afforded a further crop of *N*-acetyl-L-phenylalanine. The total yield was 8·7 g. (43% from tyrosine), and the product had m. p. 170—171°, $[\alpha]_D^{22}$ +47·6° (*c* 1 in ethanol) (lit.,[8] +47·5°, m. p. 171—172°).

L-*Phenylalanine Ethyl Ester Hydrochloride.*—A solution of *N*-acetyl-L-phenylalanine (2·0 g.) in ethanol (50 c.c.), originally saturated with hydrogen chloride, was boiled for 5 hr. and then evaporated. Crystallisation of the residue from ethanol–ether afforded 1·75 g. (79%) of the ester hydrochloride, m. p. 150—151°, $[\alpha]_D^{22}$ −7·7° (*c* 4 in water) (Found: C, 57·4; H, 7·0. Calc. for $C_{11}H_{16}O_2NCl$: C, 57·5; H, 7·0%).

N-*Acetyl*-O-(*di*-O-*ethylphosphoryl*)-L-*tyrosine Methyl Ester.*—Triethylamine (2·75 c.c.) and diethyl phosphorochloridate [9] (3·35 g.) were added to a solution of *N*-acetyl-L-tyrosine methyl ester [10] (4·5 g.) in dry acetonitrile (35 c.c.). After 30 hr. the precipitated triethylamine hydrochloride was removed and the solvent was evaporated. The gum (5 g.) which was obtained after removal of some more salt and unchanged ester (0·8 g.) crystallised from ether in colourless needles, m. p. 83° (Found: C, 51·3; H, 6·1; N, 3·8. $C_{16}H_{24}O_7NP$ requires C, 51·4; H, 6·5; N, 3·8%). This *phosphate* (1·0 g.) was reduced with sodium (0·13 g.) in liquid ammonia (20 c.c.), and the product was hydrolysed with concentrated hydrochloric acid before examination by paper chromatography; ninhydrin revealed seven spots with R_F 0·08 (weak), 0·24 (strong), 0·37 (strong), 0·43 (strong, tyrosine), 0·58 (strong, phenylalanine), 0·67 (weak), 0·84 (strong).

[7] Cf. Atherton and Todd, *J.*, 1947, 674; Steinberg, *J. Org. Chem.*, 1950, **18**, 637.
[8] Overby and Ingersoll, *J. Amer. Chem. Soc.*, 1951, **73**, 3365.
[9] McCombie, Saunders, and Stacey, *J.*, 1945, 381.
[10] Jackson, *J. Amer. Chem. Soc.*, 1952, **74**, 838.

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N-Acetyl-L-tyrosine Amide.—A solution of *N*-acetyl-L-tyrosine methyl ester (8 g.) in ammonia (200 c.c.) was kept at −40° for 5 days. The *amide* recrystallised from ethanol in prisms (5·5 g., 73%), m. p. 220—225° (Found: C, 59·1; H, 6·0; N, 12·8. $C_{11}H_{14}O_3N_2$ requires C, 59·45; H, 6·35; N, 12·6%). Phosphorylation and subsequent reduction of the gummy phosphate followed the pattern of the foregoing experiments and the final result was apparently identical.

N-Acetyl-L-tyrosine Benzyl Ester.—The preparation from L-tyrosine benzyl ester hydrochloride [11] (8·88 g.), sodium carbonate (8·2 g.), and acetyl chloride (3·45 g.) was like that of the methyl ester,[10] and crystallisation from ether–benzene gave 7·8 g. (86%) of the *benzyl ester*, m. p. 93—94°, $[\alpha]_D^{22}$ +27·9 (*c* 4 in ethanol) (Found: C, 69·0; H, 6·0; N, 4·4. $C_{18}H_{19}O_4N$ requires C, 69·0; H, 6·1; N, 4·5%). Phosphorylation and reduction with sodium in liquid ammonia was carried out as in the two foregoing instances, but the final acidic hydrolysis was omitted; instead *N*-acetyl-L-phenylalanine, m. p. 170°, $[\alpha]_D^{25}$ +47·5° (*c* 1 in ethanol) (36%), was isolated after destruction of *N*-acetyltyrosine with alkaline permanganate.

Phosphorylation and Reduction of N-Acetyl-L-tyrosine.—Hydrogenolysis of its benzyl ester with palladised charcoal in methanol containing a trace of acetic acid yielded *N*-acetyl-L-tyrosine, m. p. 153—154°, $[\alpha]_D^{25}$ +53·1° (*c* 3 in methanol), identical with that prepared in the usual way.[12] A solution of this compound (6·0 g.) in 2N-sodium hydroxide (27 c.c.) and water (50 c.c.) was brought to pH 10·0 with 2N-hydrochloric acid and then tetraethyl pyrophosphate (7·5 c.c.) was added all at once. By means of an automatic titrator delivering 2N-sodium hydroxide, the pH was maintained at 10·0 during 4 hr. Extraction of the acidified solution with ethyl acetate (3 × 40 c.c.) furnished a colourless syrup which was dissolved in dry ether (15 c.c.) and liquid ammonia (15 c.c.). This solution was added dropwise during 5 min. to a stirred solution of sodium (2·5 g.) in ammonia (50 c.c.). The *N*-acetylphenylalanine (2·05 g., 37%) which was isolated in the usual way after destruction of the *N*-acetyltyrosine with alkaline permanganate, had consistently on repetition m. p. 168—169°, $[\alpha]_D^{22}$ +45·2° (*c* 5 in ethanol). Runs under slightly varied conditions gave the same result.

O-(*Di*-O-*ethylphosphoryl*)-N-*toluene*-p-*sulphonyl*-L-*tyrosine.*—Tetraethyl pyrophosphate (0·6 c.c.) was added to a solution of *N*-toluene-*p*-sulphonyl-L-tyrosine [13] (0·55 g.) in N-sodium hydroxide, (6·0 c.c.). After 5 min. the solution was acidified and extracted with ethyl acetate (2 × 20 c.c.), which was dried, concentrated to 10 c.c., and then kept for 2 days at −5° while starting material (0·2 g.) separated. Crystallisation of the remainder from ethyl acetate–light petroleum yielded colourless needles (0·22 g., 30%) of the *phosphate*, m. p. 107°, $[\alpha]_D^{22}$ +10° (*c* 2 in ethanol) (Found: C, 51·0; H, 5·6; N, 3·15. $C_{20}H_{26}O_8NSP$ requires C, 51·0; H, 5·6; N, 3·0%). This compound (0·22 g.) was reduced with sodium (0·045 g.) in liquid ammonia (20 c.c.), and the product was desalted by anion- and cation-exchange columns; judged by paper chromatography it was entirely phenylalanine.

Phosphorylation and Reduction of L-Tyrosine.—Tetraethyl pyrophosphate (8·0 g.) was added in one portion to a stirred solution (pH 10·5) of L-tyrosine (3·62 g.) in 2N-sodium hydroxide (10 c.c.) and water (50 c.c.). By means of an automatic titrator delivering 2N-sodium hydroxide, the pH was maintained during 1 hr. at 10·5 before being brought to 7·0. The residue from evaporation of the solution was dissolved in liquid ammonia (50 c.c.) and added gradually to a solution of sodium (1·38 g.) in liquid ammonia (50 c.c.). The blue colour was discharged with ammonium chloride before the ammonia was allowed to evaporate. A solution of the residue in 5N-hydrochloric acid (100 c.c.) was boiled during 8 hr., made alkaline, and boiled again to drive off ammonia. The solution was then brought to pH 11·0 and acetylated in the usual way. After destruction of the *N*-acetyltyrosine, 0·35 g. (8·4%) of *N*-acetyl-L-phenylalanine, m. p. 169—170°, $[\alpha]_D^{21}$ +47·1° (*c* 2 in ethanol), was isolated.

The earlier part of this work was done in the University Chemical Laboratory, Cambridge, and we are grateful to Sir Alexander Todd for his generous encouragement. We also thank Dr. B. F. Erlanger, Columbia University, who had the same idea, for leaving this problem to us, the Department of Scientific and Industrial Research for a Maintenance Grant (to R. S. C.), Parke, Davis and Co. for generous support, and Albright and Wilson Ltd. for gifts of phosphorus compounds.

UNIVERSITY OF LIVERPOOL. [*Received, July 3rd,* 1959.]

[11] Erlanger and Hall, *J. Amer. Chem. Soc.*, 1954, **76**, 5781.
[12] Du Vigneaud and Meyer, *J. Biol. Chem.*, 1932, **98**, 305.
[13] Fischer and Lipschitz, *Ber.*, 1915, **48**, 375.

823. *Diazonium Salt–Diazoate Equilibria.*

By R. J. W. Le Fèvre, R. Roper, and I. H. Reece.

Equilibria reached in alkaline aqueous media by the normal diazoates from aniline, *p*-chloroaniline, and sulphanilic acid, and by the isodiazoates from the three nitroanilines and sulphanilic acid, have been studied photometrically in relation to pH. A consistent scheme for the transformations involved is proposed (p. 4109).

This paper deals with diazonium salt–diazoate equilibria, a subject which has received little attention since the time of Hantzsch.[1-3] The experiments recorded form part of a programme initiated to provide quantitative data on the interconversions of n- and iso-diazoates and their common precursors, diazonium cations. In addition to questions of structure, details of the pH-dependent appearances of these and related species were obviously important. A few years ago relevant data were sparse (cf. ref. 4, p. 102, and pp. 378—399). Since then, the kinetics of a n- to iso-diazoate transformation in aqueous sodium hydroxide have been examined,[5] and ultraviolet spectral changes associated with pH and structure noted.[5,6] The present work utilises the absorption differences between the individuals involved to obtain equilibrium results for the n-diazoates from aniline, *p*-chloroaniline, and sulphanilic acid, and for the isodiazoates from the three nitroanilines and sulphanilic acid. More recently, Lewis and Suhr[7] have published observations, also spectrophotometric, of the *p*-nitrobenzene isodiazoate–diazonium salt system, and Wittwer and Zollinger[8] have described a potentiometric study of the equilibria $RR'C_6H_3{\cdot}N_2^+ + 2OH^- \rightleftharpoons RR'C_6H_3{\cdot}N{:}N{-}O^- + H_2O$ (where R and R′ were H, 3-SO_3^-; H, 4-Cl; or 4-Cl, 2-SO_3^- respectively). Comments on these contributions are made below.

Experimental

Preparation of Materials.—Diazonium salts and diazoates were prepared by standard methods given in refs. 4—6.

Buffer Solutions.—Phosphate, borate, and potassium hydrogen phthalate buffers, covering the pH range 4—12, were made up as prescribed by Manov *et al.*,[9,10] Vogel,[11] and Clark.[12] The Marconi TF 717A pH meter, used with glass electrodes, was standardised at pH 4·01 and 9·18 by 0·05M-potassium hydrogen phthalate and 0·01M-borax, respectively.[13] Measurements, all at 25°, were taken in triplicate, and their means accepted. Check calibrations were made between each set; reproducibility was ±0·02 unit (or ±0·03 with the special electrode for highly alkaline solutions).

Spectra.—Solutions of either a diazonium salt in 0·1N-hydrochloric acid or a diazoate in 0·1N-aqueous sodium hydroxide were diluted extensively with the appropriate buffer solution, and spectra of equilibrium mixtures recorded (Cary or Spectracord instruments). The ionic strengths of the solutions were calculated, and simple Debye corrections[14] applied to the derived equilibrium constants. The wavelengths and extinction coefficients of the three major types of solute are given in Table 1.

[1] Hantzsch, "Die Diazoverbindungen," Ahren's Sammlung, 1903, **8**, 1.
[2] Hantzsch and Reddelien, "Die Diazoverbindungen," Springer, Berlin, 1921.
[3] Moore, Hantzsch Memorial Lecture, *J.*, 1936, 1051.
[4] Saunders, "The Aromatic Diazo-compounds and their Technical Applications," Arnold, London, 2nd Edn., 1949.
[5] Le Fèvre and Sousa, *J.*, 1955, 3154.
[6] *Idem*, *J.*, 1957, 745.
[7] Lewis and Suhr, *J. Amer. Chem. Soc.*, 1958, **80**, 1367.
[8] Wittwer and Zollinger, *Helv. Chim. Acta*, 1954, **37**.
[9] Manov, De Lollis, and Acree, *J. Res. Nat. Bur. Stand.*, 1945, **34**, 115.
[10] Manov, De Lollis, Lindvall, and Acree, *ibid.*, 1946, **36**, 543.
[11] Vogel, "Text-book of Quantitative Inorganic Analysis," Longmans, Green and Co., 2nd Edn., 1951, 870.
[12] Clark, "The Determination of Hydrogen Ions," Baillière, Tindall and Co., London, 1928, 209.
[13] Robinson and Stokes, "Electrolyte Solutions," Butterworths, London, 1955, 357.
[14] Eastman and Rollefson, "Physical Chemistry," McGraw-Hill, 1st Edn., 1947, 373.

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TABLE 1. *Wavelengths and extinction coefficients used in equilibria measurements.*

Substituent in parent aniline	Diazonium salt (0·1N-HCl)	n-Diazo-component (0·1N-NaOH)	Isodiazo-component (0·1N-NaOH)
H	262(12,390)	262(2350)	—
p-Chloro-	282(16,750)	282(2860)	—
o-Nitro-	220(19,400)	—	—
	277(5890)	—	242(12,500)
m-Nitro-	229(23,300)	—	271(17,100)
	290—300(1480)	—	—
p-Nitro-	260(16,560)	—	330(13,430)
p-Sulphonoxy-	268(15,550)	268(3710)	279(11,510)

RESULTS

General.—Alteration of the alkalinity or acidity of the medium produced modifications in the spectra consistently with the following scheme:

$$\text{Diazonium salt (0·1N-HCl)} \underset{\text{H}^+\text{ (fast)}}{\overset{\text{OH}^-\text{ (fast)}}{\rightleftharpoons}} \text{n-Diazoate (0·1N-NaOH)}$$

$$\text{Diazonium salt (0·1N-HCl)} \xrightarrow[\text{H}^+\text{ (slow)}]{} \text{Isodiazoate (0·1N-NaOH)}$$

For the nitro-derivatives, where solid normal diazoates cannot be isolated, observations suggested:

$$\text{Diazonium salt (0·1N-HCl)} \underset{\text{H}^+\text{ (slow)}}{\overset{\text{OH}^-\text{ (slow)}}{\rightleftharpoons}} \text{Isodiazoate (0·1N-NaOH)}$$

Early experiments showed that the spectral changes were quantitative and that the Beer–Lambert laws were obeyed.

Equilibria involving Isodiazoates.—It being assumed that the absorption spectrum obtained from a solution of diazonium salt in 0·1N-hydrochloric acid is that of pure " diazonium " component, and that obtained from a solution of potassium isodiazoate in 0·1N-sodium hydroxide is that of pure " diazo " component, and the ultraviolet absorptions of equilibrium mixtures being measured at two wavelengths (Table 1), the ratio log [diazo-component]/[diazonium component] was calculated and plotted against pOH for solutions of various pH. Since attainment of equilibrium is slow, and since the equilibrium may be disturbed by the irreversible decomposition * $ArN_2^+ + OH^- \longrightarrow ArOH + N_2$, the equilibrium curves were treated by the method of Dewar and Urch.[15] Those curves which did not yield a linear plot for optical density/$E^m_{\text{diazo-component}}$ *vs* $E^m_{\text{diazonium component}}/E^m_{\text{diazo-component}}$ for various wavelengths, thereby indicating the presence of a third absorbing component, were rejected.

TABLE 2. *Results for the equilibrium* $o\text{-}NO_2\cdot C_6H_4\cdot N_2^+ + OH^- \rightleftharpoons$ iso-$o\text{-}NO_2\cdot C_6H_4\cdot N{=}N\cdot OH$.*

pH	log [diazo]/[diazonium]	log K_0	log K_0'	pH	log [diazo]/[diazonium]	log K_0	log K_0
9·02	1·42	6·66	11·64	7·89	0·19	6·53	12·64
8·80	1·15	6·61	11·81	7·78	0·23	6·56	12·78
8·80	1·13	6·59	11·79	7·74	0·27	6·66	12·92
8·60	0·89	6·54	11·94	7·17	−0·47	6·46	13·29
8·42	0·72	6·55	12·13	7·12	−0·36	6·62	13·50
8·16	0·62	6·70	12·53	7·12	−0·45	6·53	13·41
7·89	0·29	6·63	12·74				

* log K_0' is the constant calculated for the equilibrium $o\text{-}NO_2\cdot C_6H_4\cdot N_2^+ + 2OH \rightleftharpoons$ iso-$o\text{-}NO_2\cdot C_6H_4\cdot N{=}N{-}O^- + H_2O$.

In all cases studied, the graph of log [diazo-component]/[diazonium component] against pOH formed a straight line having slope unity. A sample plot is shown in Fig. 1, together with typical equilibrium data in Table 2.

* Cf. Lewis and Suhr.[7] The absorption spectra of decomposed solutions resemble fairly closely those of the corresponding phenols, and the evolution of nitrogen can be observed.

[15] Dewar and Urch, *J.*, 1957, 345.

Such data show the equilibrium measured to be concerned with one hydroxyl group—possibly the following:

$$X{\cdot}C_6H_4{\cdot}N^+{\equiv}N + OH^- \rightleftharpoons \text{iso-}X{\cdot}C_6H_4{\cdot}N{=}N{-}OH \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

Lewis and Suhr [7] ascribe the observed initial rapid decrease caused in the ultraviolet absorption at 340 mμ by the acidification of potassium *p*-nitrobenzeneisodiazoate to the equilibrium

$$\text{iso-}p\text{-}NO_2{\cdot}C_6H_4{\cdot}N{=}N{-}O^- + H^+ \rightleftharpoons \text{iso-}p\text{-}NO_2{\cdot}C_6H_4{\cdot}N{=}N{-}OH$$

and the subsequent slower decrease in absorption to the equilibrium (1) above. On examining this point we find that the first-order loss of diazo-component at 330 mμ, calculated on the assumption that the curve obtained for *p*-nitrobenzeneisodiazoate in 0·1N-sodium hydroxide

FIG. 1. *p-Nitroaniline derivatives.*

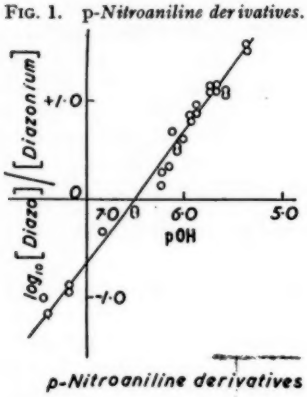
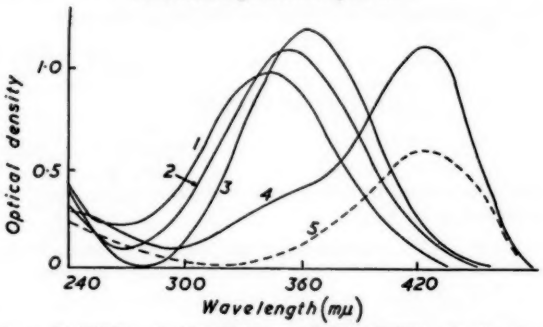


FIG. 2. *Potassium p-nitrobenzeneisodiazoate spectra in concentrated potassium hydroxide.*



1, *ca.* 6N-KOH. 2, 12N-KOH. 3, ⩾12N-KOH. 4. *As curve 3, but after 60 hr.* 5. p-*Nitrophenol in* ⩾12N-KOH.

represents pure diazo-component, can be extrapolated to intersect at zero time at a point corresponding to the initial concentration of diazo-component calculated on the same assumption. If the absorbing species after the initial rapid change were different, in fact one having a much lower absorbance at this wavelength, such a linear extrapolation could not be realised. The initial rapid change in absorbance is simply a result of the exponential nature of the concentration change.

To test whether or not the principal absorbing species in solutions of isodiazoates in dilute alkali is the isodiazohydroxide, spectra for these materials were determined in increasingly concentrated alkali solutions. For the potassium *p*-nitrobenzeneisodiazoate the curves obtained are shown in Fig. 2. Similar, but much smaller, changes were observed for other diazoates. The absorption spectrum of potassium benzeneisodiazoate in >10N-alkaline lithium iodide showed no change in either maximum wavelength or intensity, indicating that the changes observed in concentrated alkali are not due to simple salt effects.

In all cases the absorption maximum was shifted to longer wavelength accompanied by increased intensity. By analogy with the observed behaviour for substituted phenols,[16] the effect can reasonably be correlated with the equilibrium

$$\text{iso-}Ar{\cdot}N{=}N{\cdot}OH \rightleftharpoons \text{iso-}Ar{\cdot}N{=}N{-}O^- + H^+ \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

The results obtained for systems involving the equilibrium (1) are shown in Table 3.

TABLE 3. *Equilibrium constants for the equilibrium* $ArN_2^+ + OH^- \rightleftharpoons$ iso-Ar·N=NOH.

Substituent	*p*-NO_2	*o*-NO_2	*m*-NO_2	*p*-$SO_2{\cdot}O^-$ *
log K_0	6·83 ± 0·11 †	6·59 ± 0·05	6·88 ± 0·05	6·72 ± 0·05

* This should be considered more as a hydrolysis constant, since the normal diazoate interferes with the forward reaction.

† The errors presented are the mean deviation. The true experimental error is probably somewhat greater than this.

[16] Doub and Vanderbelt, *J. Amer. Chem. Soc.*, 1947, **69**, 2714, 2997; 1949, **71**, 2414.

Equilibria involving n-Diazoates.—Engler and Hantzsch,[17] and more recently, Wittwer and Zollinger,[8] have indicated that conversions of the type diazonium ion $\rightleftharpoons$ n-diazoate ion are rapid. Our own observations support this. The decomposition of diazonium compounds in alkaline solutions is also known to be faster than that of the corresponding iso-diazo-derivatives (Saunders, ref. 4, p. 99).

With the same assumption concerning the pure components as for the isodiazoates, the ultraviolet absorptions of equilibrium mixtures were measured at a single wavelength by extrapolation to zero time. Again, log {[diazo-component]/[diazonium component]} was calculated, and plotted against pOH.

For the two substituted derivatives, straight-line plots with slope 2 were obtained (Fig. 3) suggesting the equilibrium

$$p\text{-X}\cdot C_6H_4\cdot N^+\equiv N + 2OH^- \rightleftharpoons n\text{-}p\text{-X}\cdot C_6H_4\cdot N{=}N{-}O^- + H_2O \quad . \quad . \quad . \quad . \quad . \quad (2)$$

For the unsubstituted aniline compounds, the curve approached unit slope, indicating the n-benzenediazohydroxide to be a weaker acid than the corresponding substituted diazohydroxides. There are signs, in the region of high pH, of a change of slope, possibly due to

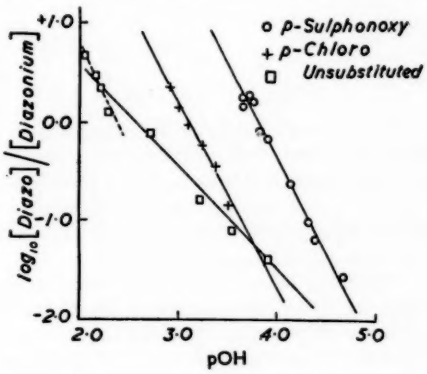


FIG. 3. *n-Diazoate–diazonium equilibria.*

○ p-*Sulphonyloxy-*. + p-*Chloro-*.
□ *Unsubstituted.*

some ionisation of a diazohydroxide, although this must necessarily be speculative, in view of the inaccuracies associated with pH determination in the range used.

The measured equilibrium constants are shown in Table 4.

TABLE 4. *Equilibrium constants* (log K_0) *involving n-diazoates at* ca. 25°.

p-X·C_6H_4·N_2^+ + 2OH$^-$ $\rightleftharpoons$ n-p-X·C_6H_4·N=N–O$^-$ + H_2O	
X = p-Cl	6·59 ± 0·04
p-SO_2·O	8·02 ± 0·08
* p-Cl	6·78 ± 0·05
p-X·C_6H_4·N_2^+ + OH$^-$ $\rightleftharpoons$ n-p-X·C_6H_4·N=N·OH	
X = p-H	2·85 ± 0·07

* Wittwer and Zollinger's value at 0° and ionic strength 0·73.

DISCUSSION

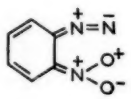
For the isodiazoate systems examined, the equilibrium constants and spectral changes observed in strong alkali indicate that these isodiazoate ions are predominantly hydrolysed to the corresponding isodiazohydroxides even in dilute alkaline solutions. The n-diazoates studied (other than the unsubstituted potassium benzene-n-diazoate) are evidently not appreciably hydrolysed in their solutions. At least for diazo-derivatives of sulphanilic acid, the normal diazohydroxide is a considerably stronger acid than the isodiazohydroxide. Such observations bring the diazohydroxides, considered as *cis*- and *trans*-isomers, into

[17] Engler and Hantzsch, *Ber.*, 1900, **33**, 2174.

line with the recorded relative acid strengths of *cis*- and *trans*-oximes and cinnamic acids (cf. Saunders,[4] p. 389) where the *trans*-compounds are invariably the weaker acids.

Furthermore, Le Fèvre and Sousa and earlier workers have observed abnormally gross differences between the ultraviolet absorption spectra of n- and iso-diazoates, compared with the corresponding differences between *cis*- and *trans*-diazo-cyanides, -sulphonates, -azobenzenes, etc. These differences need no longer be considered anomalous, since the present work shows the main absorbing species in dilute alkaline solutions of n- and iso-diazoates to be the n-diazoate ion and the isodiazohydroxide respectively. The spectra attributed by Lewis and Suhr to the *p*-nitrobenzenediazohydroxide might equally well be interpreted as those of a mixture of diazonium salt and diazohydroxide.

Quantitatively, the measured equilibrium constants (eqn. 1) for the *m*- and *p*-nitro-isodiazo-systems are the same within experimental error. This is as expected in view of the stronger conjugative $-T$ effect of the diazonium ion [18] than of the nitro-group. For the *o*-nitroisodiazo-equilibrium, steric interaction between the nitro- and the diazonium group would reduce the contribution of the form:



to the mesomeric state of the diazonium ion; this, together with the now more important inductive effect of the *o*-nitro-group, should enhance the positive nature of the diazonium nitrogen atom and thus facilitate nucleophilic attack by a hydroxyl group, resulting in a smaller equilibrium constant. The measured constant for the *p*-sulphonyloxy-compounds also is slightly less than for the *p*- and *m*-nitro-compounds, consistently with the weaker inductive effect from this group.[19]

Attempts to measure equilibrium constants with substituents of different polar type failed owing to the more rapid decomposition of these compounds. However a constant for the *p*-chlorobenzenediazonium ion–diazoate equilibrium was obtained by Wittwer and Zollinger, using a titration technique. Their value, when converted to our basis, is $\log K = 6{\cdot}78 \pm 0{\cdot}05$,* at 0° and for solutions of ionic strength 0·73. With use of values for the heat of reaction as listed by Saunders (ref. 4, p. 353) and an integrated form of the van't Hoff equation and with a Debye ionic-strength correction, Wittwer and Zollinger's equilibrium constant reduces to 6·80, agreeing satisfactorily with our value of 6·59.

That the substituted n-diazohydroxides should be stronger acids than the unsubstituted benzene-n-diazohydroxide is to be expected from the electron-withdrawing nature of the substituents. The isodiazoate results show that the strong mesomeric effect from the diazonium group swamps any electropolar effect from the substituent group. The chlorine atom, however, can exert a $+T$ effect which will be enhanced by the $-T$ effect of the diazonium group (Ingold,[19] p. 801). The tendency is towards attainment of neutrality of the $-N_2^+$ group, and consequently to a smaller equilibrium constant for the chloro-derivative than for the sulphanilic acid equilibrium.

The kinetic results of Lewis and Suhr [7] can be reconciled with present observations concerning the *p*-nitrobenzene–isodiazoate transformations and equilibria. Our experiments indicate that the overall reaction of the *p*-nitrobenzenediazonium ion with dilute alkali is

$$p\text{-}NO_2\cdot C_6H_4\cdot N^+\equiv N + OH^- \underset{k_+}{\overset{k_-}{\rightleftharpoons}} \text{iso-}p\text{-}NO_2\cdot C_6H_4\cdot N{=}N\cdot OH$$

* In the cited paper the value quoted for $(pK_1 + pK_2)/2$ is 10·61 and in another section of the paper, 11·61. Our result agrees with the value 10·61.

[18] Bolto, Liveris, and Miller, *J.*, 1956, 750; cf. Miller, *Rev. Pure Appl. Chem.* (*Australia*), 1951, **1**, 171.

[19] Ingold, "Structure and Mechanism in Organic Chemistry," Cornell Univ. Press, New York, 1953, 298, 801.

To explain the variation of the second-order rate constant k_2 with pH, Lewis and Suhr derived the equation $k_2 = k_+ + k_-/[OH^-]^2$. If the reaction followed is the above, the corresponding equation will be $k_2 = k_+ + k_-/[OH^-]$. Lewis and Suhr's rate data being used, a plot of k_2 against $1/[OH^-]$ gives a good straight line for all but one point at pH 7·01. It may be noted that Saunders (ref. 4, p. 99) shows graphically that *p*-nitrobenzeneisodiazoate has minimum stability at pH 7. To quote Lewis and Suhr " Since the reaction is not complete in much of this region, lower accuracy is to be expected from the smaller change in absorbance "—that is, at low pH. Although the calculated value of k_- ($1{\cdot}14 \times 10^{-4}$) differs from their experimental figure for the unimolecular decomposition of diazohydroxide ($2{\cdot}3 \times 10^{-3}$), the ratio k_+/k_- deduced from this graph gives an equilibrium constant, log $K = 6{\cdot}86$, in accord with that from our results, *viz.*, log $K = 6{\cdot}83$.

For the reaction of the *p*-nitrobenzeneisodiazoate with acid, if this is

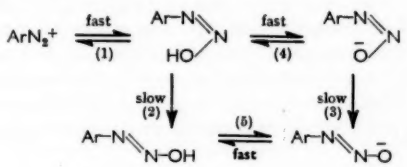
$$\text{iso-}p\text{-}NO_2{\cdot}C_6H_4{\cdot}N{=}NOH \longrightarrow p\text{-}NO_2{\cdot}C_6H_4{\cdot}N^+{\equiv}N + OH^-$$

the following equation can be derived:

$$\log k_{obs.} = \log (1 + k_+/k_- \,.\, [OH^-]) + \log k_-$$

Using our experimental value of $6{\cdot}76 \times 10^6$ for k_+/k_- and the rate data of the American authors (excluding rate constants for citrate–phosphate buffers), we can plot log $(1 + k_+/k_- \,.\, [OH^-])$ against log $k_{obs.}$. The curve deviates considerably from linearity in the region of low pH. The intercept at log $(1 + k_+/k_-[OH]) = 0$ gives a value $k_- = 2{\cdot}5 \times 10^{-3}$. Lewis and Suhr's experimental value is $2{\cdot}3 \times 10^{-3}$.

Conclusions.—A consistent scheme for the diazonium–isodiazoate transformations under study can be written as follows:



It is likely that reaction (1) is generally fast in view of the rapid coupling of normal diazoates together with the fact that coupling is known to proceed *via* the diazonium ion (cf. Ingold, ref. 19, p. 297). For unsubstituted derivatives our studies have shown its rapidity; substitution by a *p*-nitro-group should enhance the positive nature of the diazonium group [19] and result in an even faster reaction.

The ultraviolet spectra in strong alkali together with the equilibrium measurements show the isodiazohydroxide to be the predominant species in equilibrium with diazonium ion. The relative amounts of n-diazohydroxide and n-diazoate ion present should be a function of the pH. At low pH the n-diazohydroxide should occur mostly, and reaction (2) be rate controlling. The dependence of n-diazohydroxide concentration on pH by virtue of equilibrium (4) accounts for the variation of the apparent first-order rate constant observed by Lewis and Suhr. At higher pH, dissociation of the n-hydroxide to the n-diazoate ion would be virtually complete, and reaction (3) rate controlling. Since diazoate-ion concentration is no longer determined by pH, the apparent first-order rate constant should also be independent of pH, as is observed.

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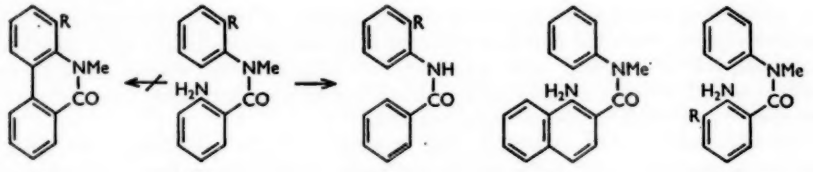
824. *Internuclear Cyclisation. Part XV.* The Catalytic Decomposition of Diazonium Chlorides prepared from* ortho-*Substituted 2-Amino-N-methylbenzanilides.*

By D. H. Hey and R. A. J. Long.

Catalytic decomposition of the diazonium chlorides prepared from three 2-amino-*N*-methylbenzanilides, which have a substituent (Me, NO_2, or OMe) at the *ortho*-position with respect to the amino-group, provide examples of demethylation and deamination without phenanthridone formation, phenanthridone formation without demethylation and deamination, and concomitant demethylation and deamination with phenanthridone formation. The factors influencing the courses of these reactions are being further investigated.

Earlier [1] it was reported that the decomposition of diazonium salts prepared from *ortho'*-substituted 2-amino-*N*-methylbenzanilides (I) did not give ring-closed products (II), but only products arising from the replacement of both the diazonium group and the *N*-methyl group by hydrogen (III). A further example of this abnormal reaction leading to simultaneous deamination and demethylation was later reported in the decomposition of the diazonium chloride prepared from *N*-(1-amino-2-naphthoyl)-*N*-methylaniline (IV), which gave 2-naphthanilide.[2] The formation of this compound from a starting compound which did not contain a substituent atom or group at the *ortho*-position to the :NMe group was unexpected. The reason for the anomalous reactions with *ortho'*-substituted *N*-methylbenzanilides was considered to be steric in character, interference between the substituent R and the *N*-methyl group causing enforced proximity of the *N*-methyl group to the diazonium group. This was considered to result in the replacement of the latter by a hydrogen atom supplied by the methyl group; it is noteworthy that the decomposition of the diazonium salt prepared from *N*-2'-amino-4',5'-methylenedioxybenzoylindoline led to the formation of a compound regarded as 4',5'-methylenedioxybenzoylindole.[3] The formation of this compound supports the view that the replacement of the diazonium group by hydrogen takes place at the expense of a methyl or methylene group attached to the nitrogen atom.



(II) (I) (III) (IV) (V)

The unexpected formation of 2-naphthanilide as a product of the decomposition of the diazonium salt prepared from *N*-(1-amino-2-naphthoyl)-*N*-methylaniline (IV) suggested that similar steric factors might be operative with a substituent atom or group at the *ortho*-position to the diazonium group in compounds derived from 2-amino-*N*-methylbenzanilides (V). Reactions have therefore been carried out with the diazonium chlorides prepared from three *N*-methylbenzanilides which carry such substituent groups. The decompositions were carried out in acid media at room temperature with the addition of copper powder.

* Part XIV, *J.*, 1959, 2254.

[1] Hey and Turpin, *J.*, 1954, 2471.
[2] Abramovitch, Hey, and Long, *J.*, 1957, 1781.
[3] Cook, Loudon, and McCloskey, *J.*, 1954, 4176.

Condensation of 3-methyl-2-nitrobenzoyl chloride with aniline gave 3-methyl-2-nitrobenzanilide, which was methylated with dimethyl sulphate to give 3,*N*-dimethyl-2-nitrobenzanilide, which was also prepared from 3-methyl-2-nitrobenzoyl chloride and methylaniline. Reduction of the 3,*N*-dimethyl-2-nitrobenzanilide gave the amine (V; R = Me), which was diazotised in the presence of hydrochloric acid and decomposed at room temperature with the addition of copper powder. 3-Methylbenzanilide was isolated together with an acidic by-product. 2-Amino-*N*-methyl-3-nitrobenzanilide (V; R = NO_2) was prepared from 3-nitroanthranilic acid and phosphorous tri-(*N*-methylanilide) by an extension of Grimmel, Guenther, and Morgan's method.[2,4] Decomposition of the diazonium chloride gave *N*-methyl-5-nitrophenanthridone and a by-product, m. p. 240°, but neither 3-nitrobenzanilide nor *N*-methyl-3-nitrobenzanilide. 3-Methoxy-2-nitrobenzanilide was prepared from 3-methoxy-2-nitrobenzoyl chloride and methylaniline. The amine (V; R = OMe) obtained on reduction was diazotised, and decomposition of the diazonium chloride gave *N*-methyl-5-methoxyphenanthridone and 3-methoxybenzanilide.

Amine (V)	Phenanthridone (%)	Demethylation and deamination (%)
R = Me	0	20
R = NO_2	13	0
R = OMe	18	5

The tabulated results obtained with these three amines indicate that factors other than steric hindrance must be involved. It is possible that the experimental conditions under which diazotisation was carried out may account in part for these results; these factors are being further investigated.

Experimental

3-Methyl-2-nitrobenzanilide.—3-Methyl-2-nitrobenzoic acid (3·7 g.), prepared by Jürgens' method,[5] was boiled under reflux with thionyl chloride (5 ml.) for 2 hr. Excess of thionyl chloride was removed under reduced pressure, and to the cold acid chloride was added pyridine (5 ml.) and then aniline (1·9 g.), After 1 hr. the mixture was heated on a water-bath. It was then poured into water and the solid which separated was crystallised from ethanol to give *3-methyl-2-nitrobenzanilide* (4·0 g.) in needles, m. p. 148—149° (Found: C, 65·1; H, 4·6. $C_{14}H_{12}O_3N_2$ requires C, 65·1; H, 4·7%).

3,N-*Dimethyl-2-nitrobenzanilide.*—(i) A solution of the above anilide (4·0 g.) in acetone (40 ml.) was boiled under reflux with sodium hydroxide (8·0 g.) in water (40 ml.), while dimethyl sulphate (8·0 ml.) was added dropwise. Boiling was continued for 20 min., after which the mixture was poured into water. Recrystallisation of the precipitated solid from ethanol gave 3,N-*dimethyl-2-nitrobenzanilide* (3·9 g.) in pale yellow needles, m. p. 123° (Found: C, 66·6; H, 5·3. $C_{15}H_{14}O_3N_2$ requires C, 66·7; H, 5·3%). (ii) To the acid chloride prepared as above from 3-methyl-2-nitrobenzoic acid (1·4 g.) was added ice-cold pyridine (5 ml.) and then *N*-methylaniline (0·83 g.). After 1 hr. the mixture was heated on a water-bath for a further hour and then diluted with water. Recrystallisation of the solid which separated gave 3,*N*-dimethyl-2-nitrobenzanilide (1·2 g.) in pale yellow needles, m. p. 123°, from ethanol identical with the product obtained by method (i).

2-Amino-3,N-dimethylbenzanilide Hydrochloride.—The nitro-compound (3·9 g.) in methanol (50 ml.) was shaken with 5% palladium–charcoal in the presence of hydrogen. When the required volume had been absorbed, the mixture was filtered and the solvent was removed under reduced pressure. The residue dissolved in ether was added to ethereal hydrogen chloride. The *amine hydrochloride* (3·3 g.) which separated crystallised from ethanol–ether in needles, m. p. 199° (Found: C, 64·8; H, 6·0. $C_{15}H_{16}ON_2$,HCl requires C, 64·8; H, 6·1%).

Decomposition of the Diazonium Chloride prepared from 2-Amino-3,N-dimethylbenzanilide.—A solution of the amine hydrochloride (3·3 g.) in concentrated hydrochloric acid (5 ml.) and water (150 ml.) was diazotised at 0° with a solution of sodium nitrite (1·0 g.) in water (10 ml.). After 1 hr. copper powder (1·0 g.) was added. Stirring was continued for 3 hr., after which the solution no longer gave a positive test with alkaline 2-naphthol. The mixture was filtered and

[4] Grimmel, Guenther, and Morgan, *J. Amer. Chem. Soc.*, 1946, **68**, 539.
[5] Jürgens, *Ber.*, 1907, **40**, 4409.

both filtrate and residue were extracted with chloroform. The combined extracts were washed with aqueous sodium hydroxide and water and then dried (Na_2SO_4). Removal of the chloroform left a pale brown gum, which was dissolved in benzene and adsorbed on an alumina column. Elution with benzene–light petroleum (b. p. 40—60°) (2 : 1; 150 ml.) gave a yellow gum (0·08 g.). Further elution with the same solvent (150 ml.) followed by benzene (250 ml.) gave a solid which on recrystallisation from aqueous ethanol afforded 3-methylbenzanilide (0·6 g.) in needles, m. p. and mixed m. p. 125° (Bachmann and Barton [6] give m. p. 125—125·5°) (Found: C, 79·6; H, 6·1. Calc. for $C_{14}H_{13}ON$: C, 79·8; H, 6·2%). Further elution of the column with benzene, and with ether–ethanol, afforded a series of pale brown gums (0·9 g.). Acidification of the alkaline washings gave a solid (0·4 g.) which crystallised from ethanol in needles, m. p. 239° (Found: C, 70·5; H, 5·7%).

2-Amino-N-methyl-3-nitrobenzanilide.—3-Nitroanthranilic acid (1·3 g.), prepared by Chapman and Stephen's method,[7] in a suspension of phosphorous tri-(*N*-methylanilide) [3] (1·3 g.) in dry toluene (50 ml.) was boiled under reflux for 2 hr. The hot solution was decanted from the metaphosphorous acid and washed successively with 2N-aqueous sodium hydroxide and 2N-hydrochloric acid. Removal of the toluene under reduced pressure left a yellow oil which solidified. Crystallisation from ethanol gave *2-amino-N-methyl-3-nitrobenzanilide* (1·4 g.) in orange prisms, m. p. 109° (Found: C, 62·2; H, 5·1. $C_{14}H_{13}O_3N_3$ requires C, 62·1; H, 4·8%).

Decomposition of the Diazonium Chloride prepared from 2-Amino-N-methyl-3-nitrobenzanilide.—The amine (2·0 g.), in ethanol (60 ml.) and concentrated hydrochloric acid (20 ml.), was diazotised with pentyl nitrite (3 ml.) at 0°. After 1 hr. the solution was diluted with cold water (120 ml.) and filtered. More water (100 ml.) and urea (2 g.) were added to the filtrate. After 10 min. copper powder (2 g.) was added. Nitrogen was evolved and a white solid began to separate. After 30 minutes' stirring the reaction was complete and the mixture was filtered. Both filtrate and residue were extracted with chloroform. The extracts were combined, washed with aqueous sodium hydroxide and with water, and dried (Na_2SO_4). Removal of the chloroform left a gum (1·8 g.), which was dissolved in a small volume of benzene and adsorbed on an alumina column. Elution with benzene–light petroleum (b. p. 40—60°) (3 : 1; 800 ml.) gave a pale yellow solid, which on recrystallisation from ethanol afforded *N-methyl-5-nitrophenanthridone* (0·25 g.) in pale yellow needles, m. p. 189° ($\lambda_{max.}$ 227, 261, 320, 333 mμ. 10^{-3} ε 49·56, 13·32, 5·27, 6·503) (Found: C, 66·2; H, 4·1. $C_{14}H_{10}O_3N_2$ requires C, 66·2; H, 4·0%). Further elution with benzene (200 ml.) and benzene–ether (1 : 1) (600 ml.) gave a yellow gum (0·1 g.), while with ether (600 ml.) and chloroform (400 ml.) a red gum was obtained from which an amorphous solid (0·3 g.), m. p. 240°, was isolated on trituration with ethanol (Found: C, 63·8; H, 4·6%). Further elution with ethanol gave a red gum (0·3 g.). Acidification of the alkaline washings gave only a trace of tar.

N-Methyl-3-nitrobenzanilide.—Pyridine (10 ml.) and methylaniline (1·3 g.) were added to 3-nitrobenzoyl chloride, prepared from the acid (2 g.) at 0°. The mixture was heated on a boiling-water bath for 1 hr. and then poured into water. Recrystallisation from ethanol of the resulting solid gave *N-methyl-3-nitrobenzanilide* (2·1 g.) in cubic crystals, m. p. 109° (Found: C, 66·5; H, 4·8. $C_{14}H_{12}O_3N_2$ requires C, 66·2; H, 4·7%). A similar procedure with aniline (1·2 g.) gave 3-nitrobenzanilide (2·2 g.) in needles, m. p. 153°.

3-Methoxy-N-methyl-2-nitrobenzanilide.—3-Methoxy-2-nitrobenzoic acid (4·0 g.) prepared by Albert and Hampton's method,[8] was boiled under reflux for 1 hr. with thionyl chloride (10 ml.). The excess of thionyl chloride was removed under reduced pressure. Pyridine (10 ml.) was added at 0° to the crude acid chloride, followed by *N*-methylaniline (2·2 g.). The solution was heated on a boiling-water bath for 1 hr. and then poured into ice–water (200 ml.). Recrystallisation of the solid which separated gave *3-methoxy-N-methyl-2-nitrobenzanilide* (4·4 g.) in pale yellow needles, m. p. 160—161°, from ethanol (Found: C, 62·8; H, 4·9. $C_{15}H_{14}O_4N_2$ requires C, 63·0; H, 5·0%).

2-Amino-3-methoxy-N-methylbenzanilide.—The nitro-compound (3·5 g.), in warm ethanol (200 ml.) containing 5% palladium–charcoal (0·5 g.), was shaken with hydrogen at atmospheric pressure. After the absorption of the required volume the mixture was filtered and the filtrate was evaporated under reduced pressure. Recrystallisation of the solid residue from ethanol

[6] Bachmann and Barton, *J. Org. Chem.*, 1938, **3**, 300.
[7] Chapman and Stephen, *J.*, 1925, 1795.
[8] Albert and Hampton, *J.*, 1952, 4988.

gave 2-*amino*-3-*methoxy*-N-*methylbenzanilide* (2·3 g.) in cubic crystals, m. p. 92—93° (Found: C, 70·5; H, 6·0. $C_{15}H_{16}O_2N_2$ requires C, 70·5; H, 6·3%).

Decomposition of the Diazonium Chloride prepared from 2-*Amino*-3-*methoxy*-N-*methylbenzanilide.*—The amine (2·2 g.), in concentrated hydrochloric acid (20 ml.) and water (100 ml.), was diazotised with sodium nitrite (1·5 g.) in water (10 ml.) at 0°. Stirring was continued for 2 hr., after which urea (2·0 g.) was added. Copper powder (1·0 g.) was added and the mixture was stirred at room temperature for 3 hr., after which a positive reaction was no longer given with alkaline 2-naphthol. The mixture was filtered and both filtrate and residue were extracted with chloroform. The combined extracts were washed with aqueous sodium hydroxide and with water and then dried (Na_2SO_4). Removal of the chloroform left a pink gum which was dissolved in benzene and adsorbed on an alumina column. Elution with benzene–light petroleum (b. p. 40—60°) (3 : 1; 900 ml.) gave only a trace of gum. Elution with benzene (400 ml.) gave a solid which, on recrystallisation from ethanol, afforded N-*methyl*-5-*methoxyphenanthridone* (0·37 g.) in needles, m. p. 163° ($\lambda_{max.}$ 238, 252, 322, 335 mμ. 10^{-3} ε 50·48, 19·38, 6·64, 11·69) (Found: C, 75·3; H, 5·4. $C_{15}H_{13}O_2N$ requires C, 75·2; H, 5·5%). Further elution with benzene–ether (1 : 1) (250 ml.) gave a solid (0·1 g.) which, on recrystallisation from benzene–light petroleum (b. p. 40—60°), gave 3-methoxybenzanilide (0·09 g.) in needles, m. p. and mixed m. p. 118° [see below]. Subsequent elution with ether (400 ml.) gave a yellow gum (0·1 g.) and with ether–chloroform (1 : 1) (400 ml.) a red gum, which on trituration with ethanol afforded a buff amorphous powder (0·1 g.), m. p. 278—279° (Found: C, 75·0; H, 6·1%).

3-*Methoxybenzanilide.*—Pyridine (8 ml.) and then aniline (1·5 g.) were added at 0° to 3-methoxybenzoyl chloride prepared from the acid (2·5 g.). The solution was heated on a boiling-water bath for 1 hr. and then poured into ice–water (100 ml.). The solid which separated crystallised from dilute ethanol to give 3-*methoxybenzanilide* (2·2 g.) in needles, m. p. 118° (Found: C, 74·1; H, 5·7. $C_{14}H_{13}O_2N$ requires C, 74·3; H, 5·9%).

3-*Methoxy*-N-*methylbenzanilide.*—In similar manner the 3-methoxybenzoyl chloride, prepared from the acid (2·5 g.), and methylaniline (1·8 g.) gave 3-*methoxy*-N-*methylbenzanilide* (2·1 g.), which separated from aqueous ethanol in prisms, m. p. 63° (Found: C, 74·7; H, 6·2. $C_{15}H_{15}O_2N$ requires C, 74·5; H, 6·4%).

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825. *Amine Compounds of the Transition Elements. Part IV.* The Reaction of Tantalum*(v) *Chloride with Some Aliphatic Amines.*

By P. J. H. CARNELL and G. W. A. FOWLES.

The reaction of tantalum(v) chloride with a number of primary, secondary, and tertiary aliphatic amines has been studied. With methylamine and ethylamine, basic aminotantalum(v) chlorides $TaCl_3(NHR)_2,3NH_2R$ are thought to be formed. Reaction with n-propylamine and n-butylamine gives compounds $TaCl_3(NHR)_2,NH_2R$, and with dimethylamine, diethylamine, and di-n-propylamine gives analogues $TaCl_3(NR_2)_2,NHR_2$; these compounds have been extracted from the reaction mixture with benzene. Trimethylamine and triethylamine form simple adducts, $TaCl_5,2NMe_3$ and $TaCl_5,NEt_3$, respectively.

The probable reaction mechanisms and the structures of the products are discussed.

RECENT investigations have shown that covalent transition metal halides undergo solvolysis when they react with liquid ammonia,[1] or with primary and secondary aliphatic amines.[2] With any specific halide, the degree of solvolysis decreases along the series NH_3,

* Part III, Fowles and McGregor, *J.*, 1958, 136.

[1] Fowles and Osborne, *J.*, 1959, 2275.
[2] Fowles and Pleass, *J.*, 1957, 2078.

NH_2R, NHR_2, and the products become increasingly soluble in organic solvents. Simple addition compounds are normally formed between the halide and tertiary amines, although prolonged interaction often results in reduction of the metal to a lower valency state.[3] While the reactions of vanadium(IV) chloride [3,4] and niobium(V) chloride [2,5] with ammonia, methylamine, dimethylamine, and trimethylamine have been examined, only the ammonolysis of tantalum(V) chloride has been studied in any detail. Lindner and Feit [6] made a brief study of the reactions of tantalum(V) chloride with several aldehydes and with one or two aromatic amines, although unfortunately they often used tantalum(V) chloride in ethanolic or acetone solution so that an enormous amount of solvolysis had occurred before reaction with the amines; these workers did not study reactions with aliphatic amines. We have accordingly extended our investigations to a fairly detailed study of the reaction of tantalum(V) chloride with primary (NH_2Me, NH_2Et, NH_2Pr^n, NH_2Bu^n), secondary ($NHMe_2$, $NHEt_2$, $NHPr^n_2$), and tertiary (NMe_3, NEt_3) amines. Analogous reactions of tantalum(V) bromide have been examined briefly.

Experimental

Materials.—Tantalum(V) chloride was prepared by passing dry gaseous chlorine over powdered tantalum metal (99·9% pure) at 300°, and purified by sublimation (Found: Cl, 48·8; Ta, 50·9. Calc. for $TaCl_5$: Cl, 49·5; Ta, 50·5%). Tantalum(V) bromide was made by the analogous reaction of bromine vapour with tantalum in an atmosphere of nitrogen (Found: Br, 68·5; Ta, 31·7. Calc. for $TaBr_5$: Br, 68·85; Ta, 31·15%). Methylamine, dimethylamine, and trimethylamine were purified as previously described.[3] Higher amines, of the best available purity, were dried by distilling them several times *in vacuo* from freshly crushed barium oxide.

Analysis.—The products were normally dissolved in anhydrous ethanol and aliquot parts taken for analysis, since aqueous solutions usually deposited part of the tantalum as insoluble hydrated tantalum(V) oxide. Many products adhered firmly to the sides of the vessel, and in such cases they were dissolved *in situ*, so that only ratios are quoted. Tantalum was determined by precipitation as hydrated oxide with tannin, followed by ignition to the oxide.[7] Nitrogen and chlorine were determined as described previously.[8] Bromine was determined by potentiometric titration with silver nitrate solution.

Magnetic Susceptibility Measurements.—These were made at room temperature on a Gouy-type balance at a field strength of 8000 gauss.

Molecular Weights.—These were measured at 20° by a modified form of the isoteniscope method.[9]

General.—Reactions were studied under completely anhydrous conditions in the usual type of all-glass closed vacuum system.[3,10] In preliminary experiments, amine was condensed on to a known weight of the halide and after reaction for several hours at room temperature the excess of amine was removed *in vacuo* at various temperatures. Experiments were also made in which the reactants were sealed in ampoules, sometimes in the presence of a solvent such as benzene, and the products were obtained by pumping off the excess of amine; where the products might be mixtures of the amine hydrochloride and a basic aminotantalum(V) chloride, separations were attempted by treatment with various solvents.

Reaction of Tantalum(V) *Chloride with Tertiary Aliphatic Amines.*—When sealed in ampoules, tantalum(V) chloride and trimethylamine reacted to give a flesh-coloured solid and a colourless solution. Evaporation of the excess of amine left a solid of composition Ta : Cl : N = 1·00 : 4·81 : 1·94. This product, which was diamagnetic, was insoluble in both trimethylamine

[3] Fowles and Pleass, *J.*, 1957, 1674.
[4] Fowles and Nicholls, *J.*, 1959, 990.
[5] Fowles and Pollard, *J.*, 1952, 4938.
[6] Lindner and Feit, *Z. anorg. Chem.*, 1923, **132**, 10.
[7] Hillebrand, Lundell, Bright, and Hoffman, "Applied Inorganic Analysis," Wiley, 2nd edn., New York, 1953.
[8] Bannister and Fowles, *J.*, 1958, 751.
[9] Weissberger, "Physical Methods of Organic Chemistry," Vol. I, Part 1, Interscience, New York, 1949, p. 173.
[10] Fowles and Pollard, *J.*, 1953, 2588.

and benzene. In the analogous reaction with triethylamine, tantalum(v) chloride formed a brown solid (Found: Ta : Cl : N = 1·00 : 4·93 : 0·99).

Reaction of Tantalum(v) *Chloride with Secondary Aliphatic Amines.*—Tantalum(v) chloride dissolved in dimethylamine to give an orange solution and a small quantity of white crystals. After excess of amine had been pumped away at 40°, an orange powder remained (Found: Ta : Cl : N = 1·00 : 4·96 : 4·98 and 1·00 : 4·93 : 4·82). When this solid was treated with benzene, an orange solution was formed, leaving a white residue; evaporation of benzene from the solution left an orange solid *adduct* (Found: Ta : Cl : N = 1·00 : 3·06 : 2·88 and 1·00 : 2·84 : 2·92) [Found: *M* 448 in benzene solution. $TaCl_3(NMe_2)_2,NHMe_2$ requires *M*, 420].

Tantalum(v) chloride reacted with diethylamine in a similar manner, although the orange product remaining after removal of excess of amine at the pump was now a thick oil, and it was probably a concentrated solution of the reaction products in excess of amine,[11] since diethylamine was slowly lost on prolonged pumping and the product had a Ta : N ratio of 1·0 : 5·5—6·6, depending on the time for which pumping was carried out. A solid product could be obtained if the initial reaction was carried out in benzene solution with only a slight excess of amine (6 $NHEt_2$: 1 $TaCl_5$). The product dissolved in benzene to an orange solution, leaving an insoluble white residue; the orange solid obtained by evaporation of benzene from the solution was analysed (typical analysis, Ta : Cl : N = 1·00 : 3·43 : 3·20). No matter how the experimental conditions were varied the Cl : Ta ratio remained greater than 3 : 1, and it seems that the extracted product is $TaCl_3(NEt_2)_2,NHEt_2$ contaminated by small amounts of diethylamine hydrochloride; thus although the hydrochloride is insoluble in pure benzene it probably dissolves slightly under the experimental conditions where a little free diethylamine is present.[3] When the initial product was washed with ethylene glycol dimethyl ether a white residue of diethylamine hydrochloride remained (Found: Cl, 32·5; N, 12·9. Calc. for $C_4H_{11}N,HCl$: Cl, 32·3; N, 12·8%).

Di-n-propylamine also reacted with tantalum(v) chloride to give an orange solution and white crystals; the white solid, which was isolated by the direct filtration of the contents of the ampoule, was shown by analysis to be di-n-propylamine hydrochloride (Found: Cl, 25·7. Calc. for $C_6H_{15}N,HCl$: Cl, 25·8).

Reaction of Tantalum(v) *Chloride with Primary Aliphatic Amines.*—Tantalum(v) chloride reacted with methylamine to give a colourless solution together with a small amount of undissolved white solid. After removal of excess of amine at the pump (12 hr. at 40°), a white solid remained with a composition Ta : Cl : N = 1·00 : 4·97 : 7·06 (duplicate 1·00 : 5·04 : 6·89). Since seven moles of methylamine were associated with each mole of tantalum(v) chloride, it seemed likely that the substance was a mixture of solvolysis products; however, no part of the product dissolved in such solvents as benzene and chlorobenzene. The product was therefore heated *in vacuo*, so that information about its composition might be obtained by a study of its thermal decomposition. Any gases liberated by the product were trapped and analysed, and the residue was weighed at all stages. In 16 hours' heating to 100° three mols. of methylamine were lost, leaving a red solid (Found: $TaCl_5,3{\cdot}98NH_2Me$); a further mol. of amine was lost when this substance was heated to 150° for 10 hr., and the residue was green (Found: $TaCl_5,3{\cdot}02NH_2Me$). More extensive breakdown occurred above 200°, a white sublimate and a dark green residue being formed. Magnetic-susceptibility measurements showed the product remaining at 150° to be diamagnetic.

In the analogous reaction between tantalum(v) chloride and ethylamine, the initial product was a pale greenish-yellow solution, which left an orange solid *adduct* on removal of excess amine (Found: Ta, 27·4; Cl, 26·5; N, 14·3. $TaCl_5,7NH_2Et$ requires Ta, 26·8; Cl, 26·3; N, 14·5%). The orange-coloured, glass-like product obtained on removal of excess of n-propylamine from the product of its reaction with tantalum(v) chloride had an analysis corresponding to a ratio Ta : Cl : N = 1·00 : 4·83 : 5·27 (and 1·00 : 4·78 : 4·83). On treatment with benzene, an orange solution was formed and a white residue of propylamine hydrochloride remained (Found: Cl, 36·7; N, 14·5. Calc. for C_3H_9N,HCl: Cl, 37·1; N, 14·7%). The orange solid remaining after evaporation of the benzene from the solution gave Ta : Cl : N = 1·00 : 2·94 : 3·00.

Tantalum(v) chloride and n-butylamine also reacted to give an orange solution and a white residue. After evaporation of excess of n-butylamine, the product was extracted with benzene to give an orange solution (Found: Ta : Cl : N = 1·00 : 2·99 : 3·12) and a white residue (Found: N, 12·7; Cl, 32·4. Calc. for $C_4H_{11}N,HCl$: N, 12·8; Cl, 32·4).

[11] Fowles and McGregor, *J.*, 1958, 136.

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Reaction of Tantalum(v) *Bromide with Aliphatic Amines.*—Tantalum(v) bromide was treated with methylamine and with dimethylamine in ampoules. The general appearance and preliminary analyses of the products showed them to be very similar to those formed by tantalum(v) chloride. These reactions were not studied further.

Discussion

Tantalum(v) chloride reacts with trimethylamine and triethylamine to give products of overall composition $TaCl_5,2NMe_3$ and $TaCl_5,NEt_3$ respectively. These products are somewhat analogous to the 1 : 1 adducts formed between diethyl ether and the chlorides and bromides of both niobium(v) and tantalum(v), which appear to be monomeric in ether solution at room temperature.[12] Although we have no evidence that the amine compounds are monomeric, it at least seems reasonable to consider them as simple adducts. The only alternatives are either that tantalum has been reduced to a lower valency state, or that solvolysis has occurred, so that $TaCl_5,2NMe_3$ for instance might be a mixture such as $TaCl_4NMe_2 + NMe_4Cl$. Reduction is extremely unlikely in view of the reluctance of tantalum to assume a valency state lower than five, and indeed the colours of the solid products and the solutions they form on hydrolysis, together with the diamagnetism of the trimethylamine product, indicate that no reduction has taken place. While solvolysis cannot be completely ruled out in the trimethylamine reaction, it is unlikely, because it requires the breaking of a strong nitrogen–carbon bond in the amine molecule. With triethylamine, the product is almost certainly a simple adduct, because either reduction or solvolysis would involve reaction with at least two molecules of the amine, and the observed composition of the product then implies that the reaction only goes just halfway despite the prolonged reaction time.

We therefore consider both products to be simple addition compounds in which tantalum(v) chloride acts as a Lewis acid and uses its vacant *5d*-orbitals to accept electrons from the nitrogen atoms of the amine ligands. Since triethylamine is a stronger base than trimethylamine [13] it is at first rather surprising that it is co-ordinated to tantalum(v) chloride to a small extent. It must be remembered, however, that steric considerations are more important that inductive effects when the reference acid is bulky,[14] so that the increased size of the triethylamine molecule accounts for its lower order of co-ordination. The compound said [6] to be formed between tantalum(v) chloride and pyridine, $TaCl_5,2py$, is presumably of a similar nature to $TaCl_5,2NMe_3$.

From our previous experience in the analogous reactions of dimethylamine with niobium(v) chloride and vanadium(IV) chloride, it was evident that the product, $TaCl_5,5NHMe_2$, formed with tantalum(v) chloride must be a mixture of aminolytic products, and we have been able to confirm this by extraction of the basic aminotantalum(v) chloride, $TaCl_3(NMe_2)_2,NHMe_2$, from the reaction mixture. $TaCl_5,5NHMe_2$ is thus the mixture, $TaCl_3(NMe_2)_2,NHMe_2 + 2NHMe_2,HCl$. This basic aminotantalum(v) chloride is monomeric in benzene solution, showing the tantalum atom to have an octahedral configuration (d^2sp^3). It is directly analogous to the previously reported niobium compound, $NbCl_3(NMe_2)_2,NHMe_2$, but differs in that the co-ordinated molecule of dimethylamine is apparently more strongly bonded to the tantalum compound; thus, unlike the niobium compound, the tantalum compound in solution does not lose its co-ordinated molecule of dimethylamine. While this seems unexpected, since tantalum(v) is rather more basic than niobium(v) and should attract electrons from the nitrogen ligands less readily, a probable explanation is that the investigations were made in different solvents (niobium in nitrobenzene, tantalum in benzene), and that the dissociation is a function of the polarity of the solvent rather than of the strength of the metal–nitrogen link.

[12] Cowley, Fairbrother, and Scott, *J.*, 1958, 3133.
[13] Hall and Sprinkle, *J. Amer. Chem. Soc.*, 1932, **54**, 3469.
[14] Brown and Taylor, *J. Amer. Chem. Soc.*, 1947, **69**, 1332.

The initial reaction takes place between solid tantalum(v) chloride and liquid dimethylamine, and it is probable that an amine molecule is first co-ordinated to the halide, hydrogen chloride being then eliminated (with excess of amine it forms dimethylamine hydrochloride). Solid tantalum(v) chloride presumably has the same dimeric bridged structure as niobium(v) chloride,[15] so that the tantalum atom must assume a co-ordination number of seven in the intermediate co-ordination stage of the reaction with dimethylamine.

A similar aminolytic reaction occurs between tantalum(v) chloride and either diethylamine or di-n-propylamine, since the appropriate amine hydrochloride has been isolated from the products. With the higher secondary amines it is more difficult to free the basic aminotantalum(v) chloride from the amine hydrochloride, but fairly pure $TaCl_3(NEt_2)_2,NHEt_2$ has been obtained. It is interesting to note that, although diethylamine is a stronger base than dimethylamine,[13] the reaction with tantalum(v) chloride proceeds no further.

It is not surprising that aminolysis should occur with secondary amines but not with tertiary amines, since a nitrogen–hydrogen bond is more readily broken than a nitrogen–carbon bond. Moreover, the reaction of tantalum(v) chloride with secondary amines closely resemble those with alcohols. Thus when tantalum(v) chloride reacts with methyl alcohol or ethyl alcohol, three tantalum(v)–chlorine bonds are solvolysed, giving $TaCl_2(OR)_3$,[16] although complete solvolysis to the alkoxide, $Ta(OR)_5$, may be effected under suitable conditions.[17] Various phenol derivatives have also been prepared,[18,19] *e.g.*, $TaCl_3(OC_{14}H_9)_2$, $TaCl_2(OC_{10}H_7)_3$, $TaCl(OPh)_4$, $Ta(OC_{10}H_7)_5$, and $Ta(OPh)_5$. As we should expect, solvolysis is normally more extensive with alcohols than with amines, because the O–H bonds yield protons more readily than do N–H bonds. It was particularly noticeable that our basic aminotantalum(v) chlorides reacted vigorously with anhydrous ethanol.

The product of the tantalum(v) chloride–methylamine reaction, $TaCl_5,7NH_2Me$, is again unquestionably a mixture of aminolytic products, although in this instance we have been unable to separate them since neither component is soluble in any solvent which will not react irreversibly with the tantalum component. Alcohols, for instance, will react to produce compounds with tantalum–oxygen bonds. The overall formula allows only three simple compositions for the reaction mixture, corresponding to the replacement of one, two, or three chlorine atoms: (i) $TaCl_4(NHMe),5NH_2Me + NH_2Me,HCl$; (ii) $TaCl_3(NHMe)_2,3NH_2Me + 2NH_2Me,HCl$; (iii) $TaCl_2(NHMe)_3,NH_2Me + 3NH_2Me,HCl$. Since dimethylamine and ammonia [20] both force the replacement of two chlorine atoms, it seems probable that methylamine reacts in the same way, *i.e.*, according to reaction (ii). Some of the three mols. of methylamine may be held in the lattice,* rather than co-ordinated directly to the tantalum atom; in the latter instance the tantalum atom has a co-ordination number of eight.

Confirmation is provided by a study of the thermal decomposition of the product *in vacuo*, which is in excellent accord with the scheme:

$$TaCl_3(NHMe)_2,3NH_2Me \longrightarrow TaCl_3(NHMe)_2 + 3NH_2Me \text{ at } 100°$$
$$\downarrow$$
$$TaCl_3(NMe) + NH_2Me \text{ at } 150°$$

Moreover, the compound evidently undergoes a fairly fundamental change upon losing the last molecule of amine, since it changes from red to green. The colour change might, alternatively, arise from the reduction of tantalum to a lower valency state, although the

* We are grateful to a referee for pointing this out.

[15] Zalkin and Sands, *Acta Cryst.*, 1958, **11**, 615.
[16] Funk and Niederländer, *Ber.*, 1929, **62***B*, 1688.
[17] Bradley, Wardlaw, and Whitley, *J.*, 1955, 726.
[18] Funk and Niederländer, *Ber.*, 1928, **61***B*, 249.
[19] Funk and Baumann, *Z. anorg. Chem.*, 1937, **231**, 264.
[20] Moureu and Hamblett, *J. Amer. Chem. Soc.*, 1937, **59**, 33.

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diamagnetism of the green product indicates that no such valency change has occurred. The magnetic properties are not complete proof, however, because the paramagnetism normally associated with the unpaired electrons might not exhibit itself at room temperature in such a magnetically concentrated material.[21] It is not possible to write down a simple scheme for the thermal decomposition if we assume that three tantalum–chlorine bonds are aminolysed in the initial reaction; it becomes necessary to propose a solid–solid back reaction between the basic aminotantalum(v) chloride and methylamine hydrochloride, which is much less likely:

$$TaCl_3(NHMe)_3,NH_2Me + 3NH_2Me,HCl \longrightarrow TaCl_3(NMe) + 2NH_2Me,HCl + 4NH_2Me$$

In the analogous reaction of niobium(v) chloride with methylamine,[2] small amounts of dimeric $NbCl_2(NHMe)_3$ were extracted from the reaction mixture, although this was not so with the tantalum product. The niobium(v) chloride–methylamine reaction was not examined further, and it was assumed that the product was entirely the mixture, $NbCl_2(NHMe)_3 + 3NH_2Me,HCl$, in which most of the basic aminoniobium(v) chloride was highly polymeric and insoluble in chlorobenzene. In view of the close similarity of niobium(v) chloride and tantalum(v) chloride, however, it seems probable that the insoluble bulk of the niobium(v) chloride reaction product contains $NbCl_3(NHMe)_2$. To clarify this point, and to obtain further structural information, work has been initiated on the reaction of niobium(v) chloride with a series of primary aliphatic amines.

Ethylamine evidently reacts with tantalum(v) chloride in a directly analogous manner to methylamine, since the initial product is again $TaCl_5,7NH_2Et$. The overall composition of the products of the reaction of tantalum(v) chloride with both n-propylamine and n-butylamine is $TaCl_5,5NH_2R$, and from these products we have been able to extract the basic aminotantalum(v) chlorides $TaCl_3(NHPr^n)_2,NH_2Pr$ and $TaCl_3(NHBu^n)_2,NH_2Bu$ respectively; the appropriate amine hydrochlorides have also been isolated. It seems that in both instances the basic aminotantalum(v) chloride co-ordinates only one mol. of amine. We attribute the solubility of the compounds in organic solvents to the increasing size of the alkyl group.

Thus we suggest that tantalum possibly assumes a co-ordination number of eight with the methylamine and ethylamine products, but that with primary amines containing larger alkyl groups or with secondary amines the increasing steric volume of the ligand lowers the co-ordination to six.

It is interesting to consider why only two of the five chlorine atoms in tantalum(v) chloride are normally replaced in reactions of the halide with ammonia or with primary and secondary aliphatic amines. It has been suggested [3] that solvolysis is limited by the inability of the partly replaced metal halide to form the intermediate compound necessary for subsequent reaction, but this is certainly not the case with the reactions of tantalum(v) chloride because all the replaced compounds co-ordinate at least one mol. of ammonia or amine. The explanation appears to be that as tantalum–chlorine bonds become replaced by tantalum–nitrogen bonds so the remaining tantalum–chlorine bonds become stronger—through an increase in their ionic character—and are less easily broken.

The tantalum(v) bromide–amine reactions were not studied in any detail because the preliminary experiments showed them to be essentially the same as the analogous reactions of tantalum(v) chloride.

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THE UNIVERSITY, SOUTHAMPTON. [*Received, July 29th*, 1959.]

[21] Selwood, "Magnetochemistry," 2nd edn., Interscience, New York, 1956, p. 174.

826. β-*Aroylpropionic Acids. Part XIII.* The Infrared and Ultraviolet Spectra of the Products of Interaction of Grignard Reagents with Succinic Anhydrides and* β-*Aroylpropionic Acids and Their Esters.*

By F. G. Baddar and (Mrs.) Adiba Habashi.

In a previous publication [1] the action of Grignard reagents on succinic anhydrides and β-aroylpropionic acids and their esters was shown to afford γγ-diarylbutyrolactones (I), 3,3-diarylprop-2-ene-1-carboxylic acids (IV), 2,2,5,5-tetra-aryltetrahydrofurans (II), and 1,1,4,4-tetra-arylbuta-1,3-dienes (III), whose structures were established by ultraviolet spectra.[2] These structures have now been confirmed by infrared spectra.

The lactones (I) showed the characteristic stretching frequency for saturated γ-lactones (1780—1765 cm.$^{-1}$) [3a] (see Table 1). This band was absent from the spectra of the tetrahydrofurans (II).

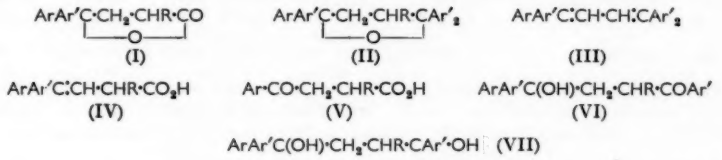
Table 1. *Infrared maxima (cm.$^{-1}$).*

Compound	R	Ar	Ar′	Alcoh. OH	OH of CO_2H	C=O of sat. lactone	C=O of CO_2H	Ketonic C=O
I*b*	Me	*o*-MeO	*o*-MeO	—	—	1775vs	—	—
c	H	2-MeO-5Me	,,	—	—	1770vs	—	—
e	H	2,5-(MeO-)$_2$	2,5-(MeO)$_2$	—	—	1780vs	—	—
f	Me	,,	,,	—	—	1775vs	—	—
g	H	2-MeO-5-Ph	*o*-MeO	—	—	1765vs	—	—
h	H	2-MeO-5-C$_6$H$_4$·OMe(-*p*)	,,	—	—	1780vs	—	—
IV*a*	Me	*o*-MeO	*o*-MeO	—	2630m	—	1715vs	—
b	H	2-MeO-5-Me	,,	—	2680m	—	1710vs	—
c	H	2-MeO-5-Cl	,,	—	2720m, 2630m	—	1710vs	—
d	H	2,5-(MeO)$_2$	2,5-(MeO)$_2$	—	2630m	—	1700vs	—
f	H	2-MeO-5-Ph	*o*-MeO	—	2600w	—	1720s	—
V*a*	Me	*o*-MeO	—	—	2660m	—	1705vs	1666vs
b	Me	2,5-(MeO)$_2$	—	—	2630w	—	1705vs	1666vs
VI*a*	H	2-MeO·C$_{10}$H$_6$(-1)	*o*-MeO	3530*m	—	—	—	1675vs
b	Me	2,5-(MeO)$_2$	2,5-(MeO)$_2$	3530*m	—	—	—	1660m
VII	H	,,	*o*-MeO	3530*m	—	—	—	—

* Sharp.

The propene acids (IV) showed the characteristic stretching frequencies of the C=O and O–H of the carboxyl group at 1720—1700 and 2700—2630 cm.$^{-1}$, respectively.[3b] The same two bands appeared in the spectra of the γ-keto-acids (V). The latter acids also showed the carbonyl stretching frequency at 1666 cm.$^{-1}$.[3c]

No characteristic bands appeared in the infrared spectra of the tetra-arylbuta-1,3-dienes (III), and their structure rest entirely on their ultraviolet spectra.[2]



The structure assigned to 1-(2,5-dimethoxyphenyl)-1,4,4-tri-*o*-methoxyphenylbutane-1,4-diol was supported by the ultraviolet spectrum,[2] and is now confirmed by a sharp infrared band at 3530 cm.$^{-1}$, characteristic of the O–H group.[3d]

The ultraviolet spectra of the γ-hydroxybutyrophenones (VI*a*, *b*, and *c*) (Figure) threw

* Part XII, submitted for publication in *Egypt J. Chem.*

[1] Baddar, El-Assal, and Habashi, *J.*, 1957, 1690.
[2] Baddar, Habashi, and Sawiris, *J.*, 1957, 1699.
[3] Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen, London, 1956, pp. (*a*) 153, (*b*) 140, (*c*) 114, (*d*) 84.

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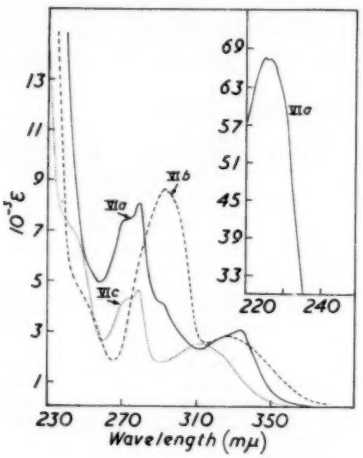
some light on the structures. Thus, compound (VI*c*) had maxima at 279 (ε 4610) and 313 mμ (ε 2520) (see Table 2) identical with those for γ-(5-chloro-2-methoxyphenyl)-γ-*o*-methoxyphenylbutyrolactone [2] ($\lambda_{max.}$ 279 mμ, ε 4630) and for *o*-methoxyacetophenone [4] [$\lambda_{max.}$ 305 mμ, ε 3800)], respectively. The absorption of this butyrophenone (VI*c*) in the region 270—280 mμ is identical with that [2] for the butanediol (VII) but with nearly half its absorption intensity. Similarly the band at 293 mμ (ε 8630) for the butyrophenone (VI*b*) is identical with that for γγ-di-2,5-dimethoxyphenyl-α-methylbutyrolactone [2] [$\lambda_{max.}$ 294 mμ (ε 7940)], whereas the band at 327·5 mμ (ε 2840) is probably due to the 2,5-dimethoxyacetophenone residue [cf. $\lambda_{max.}$ 333 mμ (ε 3640) for β-2,5-dimethoxybenzoyl-α-methylpropionic acid (V*b*)] (Table 2). The inflexions at about 240 and 245 mμ in the



Ultraviolet absorption spectra of butyrophenones (VI).

absorption curves for the ketones (VI*a* and *b*) may be equivalent to the maxima at 246 and 249 mμ of *o*-methoxyacetophenone [4] and β-2,5-dimethoxybenzoyl-α-methylpropionic acid, respectively. The absorption curve for the butyrophenone (VI*a*) shows the characteristic bands for naphthalene [5] ($\lambda_{max.}$ 225 and 280 mμ, Table 2) with a slight bathochromic shift

TABLE 2. *Ultraviolet maxima and minima* (mμ).

Compound	R	Ar	Ar′	$\lambda_{max.}$ *	ε	$\lambda_{min.}$	ε
V*b*	Me	2,5-$(MeO)_2$	—	249, 333	5880, 3640	240, 275	5220, 256
VI*a*	H	2-MeO·$C_{10}H_6$(-1)	*o*-MeO	225, 273i	67610, 7440	258·5	4930
				280, 290i	8070, 4160	313	2280
				334	3070		
b	Me	2,5-$(MeO)_2$	2,5-$(MeO)_2$	245i, 293	5010, 8630	265·5	1830
				327·5	2840	315	2570
c	H	2-MeO-5-Cl	*o*-MeO	240i, 279	7290, 4610	260	2650
				313, 274i	2520, 4300	293	1820

* = inflexion.

(5 mμ) probably due to the 2′-methoxyl group. The long-wavelength band at 334 mμ is probably the summation of two superimposed bands, a strong band for *o*-methoxyacetophenone and a weak one for substituted naphthalene. However, the curves for the three butyrophenones are identical in general features, supporting assignment of similar structures to them. These structures were confirmed by infrared spectra, compounds (VI*a* and *b*) showing the characteristic stretching frequency for the carbonyl group [3c] at 1675 and 1660 cm.$^{-1}$, respectively, and a sharp band at 3530 cm.$^{-1}$ for the O–H group.[3d]

[4] Morton and Stubbs, *J.*, 1940, 1347.
[5] Mayneord and Roe, *Proc. Roy. Soc.*, 1935, *A*, **152**, 299.

Experimental.—Infrared spectra were kindly determined by Samuel P. Sadtler and Sons, Inc., using the potassium bromide wafer technique.

Ultraviolet spectra are for solutions in 95% alcohol, measured by a Bechmann DU quartz spectrophotometer.

No infrared maxima at the regions cited were given by the tetrahydrofurans (II) where (i) R = Me and Ar = Ar′ = *o*-MeO·C_6H_4 or 2,5-$(MeO)_2C_6H_3$ or (ii) R = H and Ar = Ar′ = 2,5-$(MeO)_2C_6H_3$ or Ar = 2-MeO-5-Cl·C_6H_3 and Ar′ = *o*-MeO·C_6H_4; or by the butadienes (iii) where Ar = 2-MeO-5-Me·C_6H_3 or 2-methoxy-1-naphthyl and Ar′ = *o*-MeO·C_6H_4.

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827. *The Preparation of Aryl 2-Acetamido-2-deoxy-β-D-galactosides.*

By R. HEYWORTH, D. H. LEABACK, and P. G. WALKER.

PHENYL and *p*-nitrophenyl 2-acetamido-2-deoxy-β-D-galactosides were required as substrates for the enzyme " N-acetyl-β-galactosaminidase." [1] Difficulties were encountered in the preparation of crystalline 2-amino-2-deoxygalactose (galactosamine) hydrochloride by the methods of Jorpes and Bergstrom [2] or Roseman and Ludowieg,[3] but a combination of the procedures of Bera, Foster, and Stacey [4] for the preparation of chondroitin sulphate and of Gardell [5] for the separation of hexosamine hydrochlorides gave the essential pure hydrochloride.

As in the successful use of acetochloroglucosamine (I) (2-acetamido-3,4,6-tri-*O*-acetyl-1-chloro-2-deoxy-α-D-glucose) in the synthesis of aryl 2-acetamido-2-deoxy-β-D-glucosides,[6] and the reported lability of acetobromogalactosamine,[7] acetochlorogalactosamine (II) (2-acetamido-3,4,6-tri-*O*-acetyl-1-chloro-2-deoxy-α-D-galactose) has been prepared and used to synthesise the required substrates by condensation with phenols in aqueous acetone under alkaline conditions (cf. Glaser and Wulwek [8]).

Our unsuccessful use of titanium tetrachloride [9] in the preparation of acetochloroglucosamine from 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-α-D-glucose (unpublished results) and the successful use of mixed penta-acetates with prolonged exposure to acetic anhydride saturated with dry hydrogen chloride [6] led to our adopting the latter procedure for the preparation of acetochlorogalactosamine.

Acetochlorogalactosamine was converted into 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-α-D-galactose hydrochloride (IV). This type of conversion is not an isomerisation (cf. Tarasiejska and Jeanloz [10]) but requires a molar addition of water and was first described in the case of acetobromoglucosamine.[11]

A brief account of part of this work has been published.[12] Tarasiejska and Jeanloz [10] have since reported the synthesis of acetochlorogalactosamine and its use in the preparation of alkyl 2-acetamido-2-deoxy-β-D-galactosides.

Experimental.—Infrared spectra were determined on potassium chloride pellets.

2-Amino-2-deoxy-D-galactose hydrochloride. Barium chondroitin sulphate was prepared, from dried bovine tracheal cartilage (100 g.) by the " simplified procedure " of Bera *et al.*[4] The

[1] Heyworth, Borooah, and Leaback, *Biochem. J.*, 1957, **67**, 21P.
[2] Jorpes and Bergstrom, *Z. physiol. Chem.*, 1936, **244**, 254.
[3] Roseman and Ludowieg, *J. Amer. Chem. Soc.*, 1954, **76**, 301.
[4] Bera, Foster, and Stacey, *J.*, 1955, 3788.
[5] Gardell, *Acta Chem. Scand.*, 1953, **7**, 207.
[6] Leaback and Walker, *J.*, 1957, 4754.
[7] Stacey, *J.*, 1944, 272.
[8] Glaser and Wulwek, *Biochem. Z.*, 1924, **145**, 514.
[9] Baker, Joseph, Schaub, and Williams, *J. Org. Chem.*, 1954, **19**, 1786.
[10] Tarasiejska and Jeanloz, *J. Amer. Chem. Soc.*, 1958, **80**, 6325.
[11] Micheel, van de Kamp, and Wulff, *Chem. Ber.*, 1955, **88**, 2011.
[12] Heyworth and Leaback, *Chem. and Ind.*, 1958, 1145.

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Infrared spectra (max. in cm.$^{-1}$).

Compounds	–OH and –NH region	$NH_3^+X^-$	*O*-Acyl	Amide I & II	Hydrochlorides	C–Hal stretching
(II)	3330	None	1740	1670, 1545	None	760
(I) [6]	3250	None	1735	1640, 1540	None	755
(IV)	None	3000—2500	1750	None	2010, 1600, 1580	None
(III) [6]	None	3000—2500	1750	None	2015, 1595, 1580	None

polysaccharide was hydrolysed with 5N-hydrochloric acid (500 ml.) under reflux for 20 hr. After decolorisation with charcoal the solution was concentrated *in vacuo* to about 25 ml. and neutralised with De-Acidite FF in the carbonate form. The neutral solution was concentrated *in vacuo* to about 5 ml. and applied to a column of Dowex 50-X8 (200—400 mesh; H^+ form). The column (45 × 3 cm.) was eluted with 0·3N-hydrochloric acid, and fractions (15 ml.) were collected at 7 min. intervals. Fractions containing pure galactosamine hydrochloride were separated from the few earlier ones containing also glucosamine hydrochloride and the few later ones containing also talosamine hydrochloride [13] and amino-acids. The galactosamine hydrochloride solutions were evaporated *in vacuo* to crystals (2·4 g.) which on re-crystallisation from water had m. p. 180°.

Acetochlorogalactosamine (II). A mixture of α- and β-penta-acetylgalactosamine was made by the zinc chloride method of Stacey [7] (yield, 63%) and 2·8 g. were dissolved and kept at room temperature for 24 hr. with acetic anhydride (12 ml.) which had been saturated at 0° with dry hydrogen chloride. The solution was cooled to 0°, re-saturated with dry hydrogen chloride,[6] and kept at room temperature for 14—21 days. The mixture was poured into chloroform (50 ml.), neutralised with cold saturated sodium hydrogen carbonate, and washed with water. The chloroform layer was dried ($MgSO_4$) and evaporated. Addition of dry ether and re-evaporation gave a crystalline product (1·3 g., 50%). Recrystallisation of *acetochlorogalactosamine* from dry ethyl acetate gave plates, m. p. 130°, $[\alpha]_D^{18}$ +138° (*c* 0·7 in $CHCl_3$) (Found: C, 44·3; H, 5·8; N, 3·9, 4·3; Cl, 9·7. $C_{14}H_{20}O_8NCl$ requires C, 46·0; H, 5·5; N, 3·8; Cl, 9·7%). It is soluble in chloroform, acetone, acetic acid, or nitromethane but insoluble in ether or cold water. The infrared spectrum (Table) shows a close similarity to that of acetochloroglucosamine (I).[6]

1,3,4,6-*Tetra*-O-*acetyl*-2-*amino*-2-*deoxy*-α-D-*galactose hydrochloride* (IV). Acetochlorogalactosamine (0·25 g.) was kept in nitromethane (5 ml.) and 2N-hydrochloric acid (0·012 ml.) for 2 days. Needles (0·088 g.) were filtered off and washed with nitromethane. Water (0·005 ml.), added to the filtrate, gave a second crop (0·016 g.). The *hydrochloride* decomposed at 150—190° and had $[\alpha]_D^{18}$ +139° (*c* 0·3 in H_2O) (Found: C, 42·7; H, 5·9; N, 3·7; Cl, 9·3. $C_{14}H_{22}O_9NCl$ requires C, 43·8; H, 5·8; N, 3·7; Cl, 9·2%). It is soluble in water or acetic acid but insoluble in chloroform or nitromethane. The infrared spectrum (Table) is similar to that of the corresponding glucosamine compound (III).[6]

p-*Nitrophenyl* 2-*acetamido*-3,4,6-*tri*-O-*acetyl*-2-*deoxy*-β-D-*galactoside*. Acetochlorogalactosamine was condensed with *p*-nitrophenol according to Leaback and Walker's directions.[6] Recrystallisation from ethanol gave the *tetra-acetyl derivative*, m. p. 184°, $[\alpha]_D^{20}$ −7° (*c* 0·5 in acetone) (Found: C, 51·3; H, 5·1; N, 5·7. $C_{20}H_{24}O_{11}N_2$ requires C, 51·3; H, 5·2; N, 6·0%).

p-*Nitrophenyl* 2-*acetamido*-2-*deoxy*-β-D-*galactoside*.—The above compound (0·134 g.) was de-*O*-acetylated by shaking it in dry methanol (5 ml.) with N-sodium methoxide (0·1 ml.), and then keeping the mixture at 5° overnight. The crystals were filtered off, stirred with acetone, filtered off, and washed with acetone and ether. The *galactosaminide* (0·069 g., 71%) was heated *in vacuo* over P_2O_5 at 100° for 16 hr. and then had m. p. 205°, $[\alpha]_D^{20}$ +19° (*c* 0·12 in H_2O) (Found: C, 47·8; H, 5·7; N, 8·3. $C_{14}H_{18}O_8N_2$ required C, 49·1; H, 5·3; N, 8·2%).

The galactosaminide is seen as a single spot (R_F 0·63) on paper chromatograms run in butan-1-ol–ethanol–water (4 : 1 : 5 by vol.; upper layer) by quenching of background fluoresence in ultraviolet light. The corresponding glucosaminide has R_F 0·65.

Phenyl 2-*acetamido*-2-*deoxy*-β-D-*galactoside*. Acetochlorogalactosamine, with phenol, gave crystalline phenyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-galactoside, m. p. 165°. This product (0·6 g.) was de-*O*-acetylated by being kept in methanol (6·5 ml.) and chloroform (6·5 ml.) with 0·1N-sodium methoxide (0·5 ml.) at room temperature for 6 hr. and then at 5°

[13] Heyworth and Walker, *Supp. Internat. Abs. Biol. Sci.*, 1958, 1—48.

overnight. The crystals were filtered off and washed with methanol to yield the galactosaminide (0·28 g. 66%), m. p. 230°.

The authors are indebted to Dr. R. K. Callow for measurements of the infrared spectra. This research has been aided by grants from the Research Fund of the University of London and the Nuffield Foundation.

THE BIOCHEMISTRY DEPARTMENT, THE INSTITUTE OF ORTHOPÆDICS,
BROCKLEY HILL, STANMORE, MIDDLESEX. [*Received, May 14th*, 1959.]

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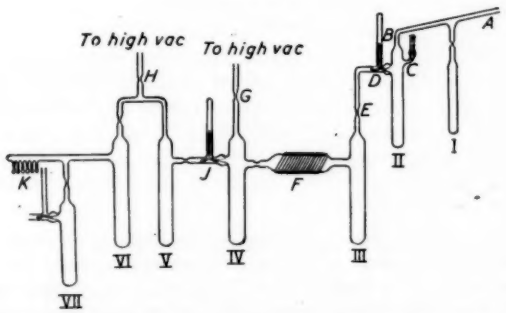
828. *The Activation of Carbon–Carbon Double Bonds by Cationic Catalysts. Part IX.*[1] *The Dimerisation of* 1,1-*Diphenylethylene in the System Benzene–Titanium Tetrachloride–Hydrogen Chloride.*

By ALWYN G. EVANS and E. D. OWEN.

DIMERISATION of 1,1-diphenylethylene in benzene–titanium tetrachloride–hydrogen chloride has been studied dilatometrically. The initial rate of dimerisation is of first order with respect to both titanium tetrachloride and hydrogen chloride, and of second order in monomer. No reaction occurs in the absence of hydrogen chloride. The product first formed is the linear dimer, 1,1,3,3-tetraphenylbut-1-ene, and this reacts further to form the cyclic dimer, 3-methyl-1,1,3-triphenylindane.

Experimental.—Titanium tetrachloride (from British Drug Houses) was refluxed over copper turnings for several days in an atmosphere of dry nitrogen, then fractionated up a 40-cm. point column, the fraction boiling at 136° being allowed to run into the high-vacuum apparatus (Fig. 1) at point *A*. A first fraction was sealed off in I, and the main distillate run

FIG. 1.



into II, which was then sealed off at *B* and *C*. The capillary at *D* was broken by the magnetic breaker, and the apparatus evacuated through *G*. After being outgassed several times, the titanium tetrachloride was distilled into III and the apparatus sealed off at *E*. The titanium tetrachloride was then distilled under high vacuum to and fro between III and IV over copper turnings in *F* kept at 150° by a heating spiral. The trap IV was then sealed off from the tube *F* and from the high-vacuum system. The rest of the apparatus was then evacuated through *H* and sealed off. The capillary *J* was broken and the titanium tetrachloride distilled *via* V and VI into the small calibrated bulbs at *K*, each of which was then sealed off. The remainder was collected and sealed off in the ampoule VII. The titanium tetrachloride so purified was perfectly colourless.

1,1-Diphenylethylene was purified as in Part V.[2] Hydrogen chloride was prepared as in Part VII.[3]

[1] Part VIII, Evans and Price, *J.*, 1959, 2982.
[2] Evans and Lewis, *J.*, 1957, 2975.
[3] Evans and Lewis, *J.*, 1959, 1946.

Benzene, purified as in Part V,[2] was sealed off for four weeks under high vacuum in vessels fitted with magnetically operated breakers and containing sodium–potassium alloy. This is liquid at room temperature, and so presented a constant untarnished surface to the benzene, which was shaken at regular intervals.

Procedure. This was the same as described in Part VII,[3] the very rigorous method *A* (Part V [2]) being used for making up all mixtures.

Results.—In the absence of hydrogen chloride, systems containing rigorously purified benzene, monomer, and titanium tetrachloride reacted at a negligible rate (see Table 1, expt.*).

TABLE 1.

10^3I.R.	10^2[HCl]	[M]	10^3[$TiCl_4$]	Temp.	10^3I.R.	10^2[HCl]	[M]	10^3[$TiCl_4$]	Temp.
a *	0	0·91	4·60	30°	1·58	2·78	0·86	4·90	55°
131	4·90	0·95	16·3	55	2·46 ‡	2·6	1·29	6·79	30
27·8	2·20	0·95	16·3	55	1·95 ‡	2·6	1·29	6·79	40
75·0	6·23	0·95	10·6	55	2·50 ‡	2·6	1·29	6·79	55
32·6	3·83	0·95	10·6	30	2·66	2·0	1·56	6·4	55
5·96	1·22	0·95	10·6	30	1·19	2·0	1·10	7·09	55
38·5 †	4·30	0·91	4·60	30	0·556	2·0	0·79	7·58	55
13·9	2·24	0·91	4·60	30	1·59	2·2	0·77	16·0	55
77·3	18·0	0·91	4·60	30	2·86	2·2	0·77	25·5	55
					89·4	2·2	0·77	721	55
					59·1	2·2	0·77	593	55

*†‡ See text. *a*, $<8 \times 10^{-5}$. I.R. = Initial rate of formation of linear dimer (moles $l.^{-1}$ $hr.^{-1}$). All concentrations molar.

On the introduction of hydrogen chloride a great increase in the reaction rate was observed (Table 1, expt.†). Thus hydrogen chloride is a cocatalyst. Part of a typical reaction curve is shown in Fig. 2; the volume was measured until its change with time became negligible.

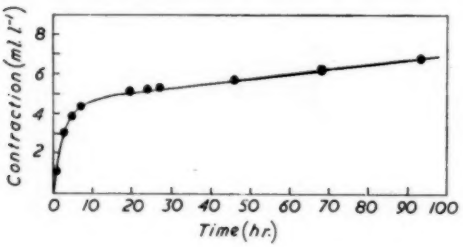


FIG. 2. *Typical reaction curve for* [Monomer] = 0·77, [$TiCl_4$] = $5·93 \times 10^{-1}$, [HCl] = $2·2 \times 10^{-2}$ moles $l.^{-1}$, *at* 55°.

Various runs were stopped at different stages and the systems analysed. When 25% of the total volume change had occurred, the product consisted entirely of 1,1,3,3-tetraphenylbut-1-ene (linear dimer), and 3-methyl-1,1,3-triphenylindane (cyclic dimer) could not be detected. At 65% of the total volume change, 85% of the product was linear dimer and 15% cyclic dimer. At 95% of the total volume change, 90% of the product was cyclic dimer and 10% linear dimer.

Initial rates of reaction found from the initial slopes of the reaction curves are shown in Table 1. Since it is the linear dimer which is formed initially, they are the rates of formation of linear dimer from monomer. The initial rate does not change with temperature over the range 30° to 55° (see Table 1, expts.‡), and so the activation energy E_l is zero.

Using the results of Table 1, we plotted log (initial rate) against log [initial monomer] for constant [$TiCl_4$] and constant [HCl]; log (initial rate) against log ($TiCl_4$) for constant [initial monomer] and constant [HCl]. We find the orders in monomer and $TiCl_4$ to be $2·2 \pm 0·2$ and $1·0 \pm 0·1$, respectively.

We have plotted log {initial rate/([initial monomer]^2[$TiCl_4$])} against log [HCl] and find that the order in HCl is $0·9 \pm 0·1$.

Thus the initial rate of formation of linear dimer = k_l[initial monomer]^2[$TiCl_4$][HCl]. The mean value of k_l at 30° is $2·3 \times 10^{-2}$ $mole^{-2}$ $l.^3$ $sec.^{-1}$.

As for the $SnCl_4$–HCl system,[3] and in contrast to the $SnCl_4$–H_2O system,[2] no optimum

[HCl]/[$TiCl_4$] ratio has been found, even though the [HCl] was increased up to 40 times that of the [$TiCl_4$], showing that no stable $TiCl_4$,HCl complex is formed.

When the colourless titanium tetrachloride is added to the benzene the resultant solution is coloured owing to complex formation between the chloride and benzene. This colour is clearly observable even for titanium tetrachloride concentrations of the order of 2×10^{-4} mole $l.^{-1}$.

Discussion.—In these monomer–$TiCl_4$–HCl–benzene systems, only linear dimer is formed at the beginning of the reaction, but later linear dimer is converted into cyclic dimer. This subsequent reaction of the linear dimer into cyclic dimer causes the volume–time curve (Fig. 2) to straighten out in the later stages.

We interpret our results in accordance with the scheme already presented in Parts VII [3] and VIII,[1] where Ti replaces Sn through eqns. (1)—(4). This mechanism will account for the results if we make the same assumptions as those of Part VIII, and the initial rate of reaction will be given by the expression:

Initial rate of formation of linear dimer $= k_{2a}[M][MH^+TiCl_5^-]$

$$= (k_{2a}k_{1a}/k_{1b})[M]^2[TiCl_4][HCl]$$

where [M] = initial monomer concentration. This expression is consistent with our results, and $(k_{2a}k_{1a}/k_{1b}) = k_{2a}K_1 = k_t$.

Values of $\Delta G_t^{\ddagger}$, $\Delta H_t^{\ddagger}$, and $\Delta S_t^{\ddagger}$ are in Table 2.

TABLE 2.

10^2k_t * ($l.^3$ mole^{-3} sec.$^{-1}$)	Temp.	$\Delta H_t^{\ddagger} = E - RT$ (kcal. mole^{-1})	$\Delta G_t^{\ddagger}$ (30°) (kcal. mole^{-1})	$\Delta S_t^{\ddagger}$ (30°) (cal. deg.$^{-1}$ mole^{-1})
2·3	30°	0	20·1	−66
1·8	40			
2·3	55			

* k_t is expressed in terms of the number of moles $l.^{-1}$ of linear dimer appearing per second.

Comparison of these results with those of Parts VII and VIII shows that the change from $SnCl_4$–HCl to $TiCl_4$–HCl (*a*) does not change the mechanism of reaction; (*b*) reduces the activation enthalpy for the conversion of monomer into linear dimer from 4·1 kcal. mole^{-1} to 0 kcal. mole^{-1}; (*c*) causes the entropy of activation to become more negative: this offsets the effect on the enthalpy of activation, and results in the value of k_t at 30° being the same for the two systems; (*d*) brings about the formation of cyclic dimer at a rate which is more comparable with that of the linear dimer formation.

The last effect is very striking.—In the case of $SnCl_4$–HCl, systems which gave a measurable rate for the conversion of monomer into linear dimer showed no production of cyclic dimer. A very high rate of production of linear dimer had to be obtained before the formation of cyclic dimer could be detected. In the case of $TiCl_4$–HCl, however, a catalyst concentration which gives a reasonable rate of formation of linear dimer also gives a reasonable rate for the production of cyclic dimer, although of course this does not begin to be measurable until the concentration of linear dimer becomes appreciable.

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UNIVERSITY COLLEGE, CATHAYS PARK, CARDIFF. [*Received, May 19th*, 1959.]

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829. *The Structures of Potassium Trifluorocuprate(II) and Potassium Trifluorochromate(II).*

By A. J. Edwards and R. D. Peacock.

Specimens of the double fluorides $KCuF_3$ and $KCrF_3$ have been prepared at various times, but apart from an observation that the unit cell of $KCuF_3$ is non-cubic [1] no structural data have been reported. In general the compounds AMF_3 (A = NH_4, K, Rb; M = transition metal) have the perowskite lattice, sometimes with slight modifications which may be the result of preparative difficulties, as none of the salts can be satisfactorily recrystallised from a solvent. Since Cu^{II} and Cr^{II} show a Jahn–Teller type of distortion in their simple fluorides,[2,3] and Cu^{II} also in the complex fluoride K_2CuF_4,[4] it is of interest to know whether similar distortions occur in the perowskite type of compound.

We find that $KCuF_3$ and $KCrF_3$ have tetragonal unit cells which for chemical reasons are assigned to space group $P4/mmm$. The unit cells (Table 1) contain one formula unit

Table 1.

Dimensions				Relative intensities			
				$KCuF_3$		$KCrF_3$	
	$KCuF_3$	$KCrF_3$	*hkl*	Calc.	Obs.	Calc.	Obs.
Unit cell size	a_0 = 4·13 Å	4·27 Å	100	12	14	8	8
	c_0 = 3·92 Å	4·01 Å	001	5	6	3·6	4·3
Density: obs.	3·97	3·31	110	22	24	20	15
calc.	3·96	3·39	101	42	42	36	29
$F_I - F_I$	2·92 Å	3·02 Å	111	5·5	5·3	8	8
$F_I - F_{II}$	2·85 Å	2·93 Å	200	29	25	28	30
Atomic positions: K at $(\frac{1}{2},\frac{1}{2},\frac{1}{2})$; Cu or Cr at (0,0,0); 3F at $(0,\frac{1}{2},0)$; $(\frac{1}{2},0,0)$; $(0,0,\frac{1}{2})$.			002	12	14	11	12
			210	2·7	3	1·6	3
			201	2·5	3	1·5	2
			102	2·2	3	1·3	1
			211	16	13	14	16
			112	7	8	6	11
			220	8	6	8	10
			202	14	14	13	16

and are closely related to the cubic perowskite cell. In each compound the transition metal has six octahedrally disposed fluorine neighbours, but the tetragonal distortion is caused by unequal metal–fluorine bond lengths; two of the six M–F distances are shorter than the other four (Table 2). The bonds are therefore distorted in a sense opposite to

Table 2. *Transition metal–fluorine distances in copper(II) and chromium(II) fluorine compounds* (Å).

CuF_2	2 at 2·27	$KCuF_3$ 4 at 2·07	K_2CuF_4 4 at 2·08
	4 at 1·93	2 at 1·96	2 at 1·95
CrF_2	2 at 2·43	$KCrF_3$ 4 at 2·14	
	2 at 2·01	2 at 2·00	
	2 at 1·98		

that found in the large majority of Cu^{II} and Cr^{II} compounds such as the difluorides, in which there are four shorter and two longer transition metal–fluorine bonds; in fact the only other example of such a distortion is in the very recently determined structure of K_2CuF_4 in which the Cu–F bond distances are nearly identical to those found by us for $KCuF_3$.

The infrared peaks for $KCuF_3$ and $KCrF_3$ [5] are out of sequence with those of the other

[1] Martin, Nyholm, and Stephenson, *Chem. and Ind.*, 1956, 83.
[2] Billy and Haendler, *J. Amer. Chem. Soc.*, 1957, **79**, 1049.
[3] Jack and Maitland, *Proc. Chem. Soc.*, 1959, 232.
[4] Knox, *J. Chem. Phys.*, 1959, **30**, 991.
[5] Peacock and Sharp, *J.*, 1959, 5545.

transition-metal perowskites (Cr, 481; Mn, 407; Fe, 431; Co, 439; Ni, 445; Cu, 489; Zn, 437 cm.$^{-1}$) and in view of the present work it seems probable that they reflect the longer M–F distances only.

Experimental.—Potassium trifluorocuprate(II) is prepared by the addition of a cupric chloride solution to a boiling solution of potassium fluoride just acidified with hydrofluoric acid. It has been reported as green, blue, or white; we find that the pure compound is a white crystalline powder (Found: K, 24·6; F, 35·9. Calc. for $KCuF_3$: K, 24·5; F, 35·7%).

Potassium trifluorochromate(II) is obtained by the addition of solid chromous acetate to potassium hydrogen fluoride solution in the absence of air. The compound, which is pale blue, is very difficult to obtain pure because it oxidises easily when wet; our specimens always contained a little potassium fluoride (Found: K, 28·2; F, 39·4. Calc. for $KCrF_3$: K, 26·4; F, 38·5%).

Thin-walled Pyrex capillaries were used to hold *X*-ray powder samples and photographs were taken with a 19 cm. Hilger camera with filtered Cu-K_α radiation. Duplicate films were microphotometered on a Hilger instrument (Type L 451); some difficulty was encountered with $KCrF_3$ because of the intense background.

The calculated intensity of a powder reflection is given by the expression

$$I_c = \text{constant} \times F^2_{hkl} \cdot \frac{1 + \cos^2 2\theta}{\sin^2 \theta \,.\, \cos \theta} \cdot pAT$$

where T is the temperature factor and the other symbols have their usual meaning. We have assumed that A and T cancel since the crystals are of moderate absorption.[6] Scattering factors were corrected for dispersion by the K electrons. Values of the scattering factors are those of Berghuis *et al.*[7]

One of us (A. J. E.) is indebted to the Department of Scientific and Industrial Research for a maintenance grant.

Department of Chemistry,
The University, Birmingham, 15. [*Received, May 29th*, 1959.]

[6] Bradley, *Proc. Phys. Soc.*, 1935, **47**, 879.
[7] Berghuis, Haanappel, Potters, Loopstra, MacGillavry, and Veenendaal, *Acta Cryst.*, 1955, **8**, 478.

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830. *Nitration of* m-*Iodonitrobenzene.*

By R. S. Kapil.

The nitration of *m*-iodonitrobenzene has been reported;[1,2] the only product isolated was 4-iodo-1,2-dinitrobenzene. We have reinvestigated this reaction. Although it might give a mixture of dinitro-isomers, only 3-iodo-[3] and 4-iodo-1,2-dinitrobenzene were isolated.

In 1-iodo-2,3-dinitrobenzene the nitro-group in position 2 is mobile and reacts with alcoholic ammonia to give 2-iodo-6-nitroaniline. The observation agrees with that of Hodgson and Smith[4] who isolated under similar conditions 2-methyl-6-nitroaniline from 2,3-dinitrotoluene. 4-Iodo-1,2-dinitrobenzene behaves normally with hydrazine hydrate, giving mainly 5-iodo-2-nitrophenylhydrazine.

Experimental.—Nitration of m-*iodonitrobenzene.* To a cooled suspension of *m*-iodonitrobenzene (10 g.) in concentrated sulphuric acid (42 c.c.; *d* 1·82), fuming nitric acid (28 c.c.; *d* 1·5) was added dropwise with vigorous shaking, the temperature being kept below 10°.

[1] Jacobson, Fertsch, and Heubach, *Annalen*, 1898, **303**, 339.
[2] Ullmann and Bielecki, *Ber.*, 1901, **34**, 2179.
[3] Wender, *Gazzetta*, 1889, **19**, 231.
[4] Hodgson and Smith, *J.*, 1933, 500.

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The mixture was heated on a water-bath for 2 hr., then poured on crushed ice. The solid mass on repeated crystallization from ethanol gave 4-iodo-1,2-dinitrobenzene as yellow plates, m. p. 74° (Found: I, 42·9. Calc. for $C_6H_3O_4N_2I$: I, 43·2%).

The mother-liquor deposited needles of 3-iodo-1,2-dinitrobenzene, which recrystallized as pale yellow needles (0·7 g.), m. p. 138° (lit.,[3] 138°), from ethanol (Found: I, 43·0%).

Action of alcoholic ammonia on 1-*iodo*-2,3-*dinitrobenzene.* The iododinitrobenzene (1 g.) in ethanol was refluxed with alcoholic ammonia for 2 hr. On cooling, 2-*iodo*-6-*nitroaniline* separated in orange-red needles, m. p. 108° (Found: I, 47·9. $C_6H_5O_2N_2I$ requires I, 48·1%).

Action of hydrazine hydrate on 4-*iodo*-1,2-*dinitrobenzene.* The iododinitrobenzene (1 g.) in ethanol was treated with 2 equiv. of cold hydrazine hydrate solution. 5-*Iodo*-2-*nitrophenylhydrazine* was filtered off after 1 hr., and recrystallized from ethyl acetate in orange-red needles (0·6 g.), m. p. 150° (Found: I, 45·3. $C_6H_6O_2N_3I$ requires I, 45·5%). It formed an *acetyl derivative*, lemon-yellow needles, m. p. 228° (from ethanol) (Found: I, 39·5. $C_8H_8O_3N_3I$ requires I, 39·6%), a *diacetyl derivative*, lemon-yellow needles or plates m. p. 172° (from ethanol) (Found: I, 34·8. $C_{10}H_{10}O_4N_3I$ requires I, 35·0%), a *propionyl derivative*, lemon-yellow needles, m. p. 162° (from ethanol) (Found: I, 37·7. $C_9H_{10}O_3N_3I$ requires I, 37·8%), and a *benzoyl derivative*, pale yellow needles, m. p. 200° (from ethanol) (Found: I, 33·1. $C_{13}H_{10}O_3N_3I$ requires I, 33·2%).

I thank Dr. S. S. Joshi, of this College, for his interest.

MEERUT COLLEGE, MEERUT, INDIA. [*Received, May 28th*, 1959.]

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831. *The Preparation of 2-Nitroacetophenone from o-Nitroaniline, and the Synthesis of 2-Phthalimidoacetophenone.*

By J. MALCOLM BRUCE and R. IAN FRYER.

SEVERAL methods[1] have been used for the preparation of 2-nitroacetophenone, but the extension of Beech's procedure[2] to this compound has not previously been described. Diazotised *o*-nitroaniline with acetaldehyde semicarbazone gave 9% of 2-nitroacetophenone semicarbazone, and with acetaldoxime gave, after hydrolysis of the intermediate oxime, 24% of 2-nitroacetophenone.

For another study, an *NN*-diacyl derivative of 2-aminoacetophenone was required. Atkinson *et al.*[3] reported that 2-diacetamidoacetophenone resulted when the amine was boiled with acetic anhydride, but in our hands this yielded only the monoacetyl derivative. Addition of a catalyst caused extensive decomposition. However, 2-phthalimidoacetophenone was obtained by treating the amine with phthalic anhydride in *NN*-dimethylformamide or acetic acid, but it was more conveniently prepared by cyclisation of 2-*o*-carboxybenzamidoacetophenone.[4]

Experimental.—Solvents were removed on the water-bath, where necessary under reduced pressure (water-pump). M. p.s are corrected.

2-*Nitroacetophenone Semicarbazone.* *o*-Nitroaniline (13·8 g.) in 6% hydrochloric acid (125 c.c.) was diazotised with sodium nitrite (7 g.) in water (15 c.c.), treated with sodium acetate (5·5 g.) in water (15 c.c.), and added during 15 min. below the surface of a stirred solution of acetaldehyde semicarbazone (15 g.), sodium acetate hydrate (54 g.), copper sulphate (5 g.), and sodium sulphite hydrate (0·8 g.) in water (140 c.c.) at 10—20°. The mixture was stirred

[1] (*a*) Kiang, Mann, Prior, and Topham, *J.*, 1956, 1319; (*b*) Reynolds and Hauser, *Org. Synth.*, 1950, **30**, 70, and references cited therein; Emerson, Heyd, Lucas, Stevenson, and Wills, *J. Amer. Chem. Soc.*, 1947, **69**, 706.
[2] Beech, *J.*, 1954, 1297.
[3] Atkinson, Simpson, and Taylor, *ibid.*, p. 165.
[4] Bogert and Nabenhauer, *J. Amer. Chem. Soc.*, 1924, **46**, 1702.

for 2 hr., then filtered, and the solid was washed with water, dried *in vacuo*, and extracted successively with boiling benzene (150 c.c.) and ethanol (150 c.c.). On being cooled the latter solution deposited a solid from which, by repeated crystallisation from ethanol, the *semicarbazone* (2 g., 9%) was obtained as bright yellow needles, m. p. 210—211° undepressed on admixture with material prepared from authentic [1a] 2-nitroacetophenone (Found: C, 48·9; H, 4·6; N, 25·3. $C_9H_{10}O_3N_4$ requires C, 48·7; H, 4·5; N, 25·2%).

2-*Nitroacetophenone*. *o*-Nitroaniline (27·6 g.) was diazotised as above, sodium acetate (17·5 g.) in water (30 c.c.) was added, and the solution was neutralised to Congo Red with hydrochloric acid. Solutions of acetaldoxime (18 g.) in water (30 c.c.), and of copper sulphate (10 g.), sodium sulphite hydrate (1·6 g.), and sodium acetate hydrate (130 g.) in water (120 c.c.), were then added simultaneously, the former below the surface, during 1 hr., and the mixture was neutralised to Congo Red, treated with concentrated hydrochloric acid (225 c.c.), and refluxed for 3 hr. Distillation in steam afforded an oil which was isolated by extraction with ether, washed with aqueous 5% sodium hydroxide, and distilled to give the nitro-ketone (8 g., 24%), b. p. 170—176°/25 mm. The semicarbazone had m. p. and mixed m. p. 209—210°.

2-*Acetamidoacetophenone*. 2-Aminoacetophenone [1a] (1·35 g.) was refluxed with acetic anhydride (5 c.c.) for 1½ hr., the solvent was removed, and the residue was distilled at 0·01 mm. (bulb-to-bulb, bath at 110°) to give an oil from which, by crystallisation from aqueous ethanol, the derivative (1·0 g.) was obtained as needles, m. p. 75° (lit.,[5] 76°) (Found: C, 67·9; H, 6·3; N, 7·8. Calc. for $C_{10}H_{11}O_2N$: C, 67·8; H, 6·2; N, 7·9%). Addition of sodium acetate or (+)-camphor-10-sulphonic acid caused extensive decompositon. Atkinson *et al.*[3] report m. p. 84—86° for 2-diacetamidoacetophenone.

2-*Phthalimidoacetophenone*. (*a*) A solution of 2-aminoacetophenone (1·35 g.) and phthalic anhydride (1·48 g.) in *NN*-dimethylformamide (10 c.c.) was heated at 100° for 1 hr., stirred, and refluxed for 2 hr., and the solvent was removed. The residue was extracted with cold benzene (20 c.c.), and the soluble material was distilled at 0·01 mm. (bulb-to-bulb, bath at 200°) to give a yellow oil which, on being crystallised from benzene–light petroleum (b. p. 40—60°), afforded the *ketone* (0·85 g., 32%) as blades, m. p. 134·5—135° (Found: C, 72·4; H, 4·3; N, 5·4. $C_{16}H_{11}O_3N$ requires C, 72·5; H, 4·2; N, 5·3%). A yield of 38% was obtained when the amine and the anhydride were refluxed together for 5 hr. with sodium acetate (4 g.) in acetic acid (20 c.c.). The 2,4-*dinitrophenylhydrazone*, orange blades from butan-1-ol, had m. p. 226° (Found: C, 59·1; H, 3·5; N, 15·7. $C_{22}H_{15}O_6N_5$ requires C, 59·3; H, 3·4; N, 15·7%).

(*b*) A mixture of 2-*o*-carboxybenzamidoacetophenone [4] (25·5 g.), sodium acetate (40 g.), and acetic acid (300 c.c.) was stirred and refluxed for 5 hr., solvent (200 c.c.) was removed, and the residue, after being cooled to 50°, was added to water (600 c.c.). The suspension was stirred for 3 hr., then filtered, and the solid was washed with water, dried, and sublimed at 130°/0·01 mm. Crystallisation of the sublimate from light petroleum (b. p. 100—120°) afforded the ketone (15·3 g., 64%), m. p. and mixed m. p. 134—135°.

One of us (R. I. F.) thanks Dr. L. Hellberg for discussions.

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[5] Davey and Gwilt, *J.*, 1957, 1008.

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832. *The Relation between the Heat and Volume of Mixing.*

By J. S. Rowlinson and A. R. Mathieson.

Mathieson [1] has recently proposed equations for the calculation of the heat of mixing from the volume of mixing of a binary mixture. His key equation, (12), relates the derivatives with respect to composition of ΔH and ΔV, where these are the differences of the molar heat and volume of the mixture and those of separated components at the same

[1] Mathieson, *J.*, 1958, 4444.

pressure and temperature. It can be most simply derived from the usual rules of partial differentiation, as follows:

$$\left(\frac{\partial \Delta H}{\partial x}\right)_{\Delta V,T} = \left(\frac{\partial \Delta H}{\partial x}\right)_{P,T} + \left(\frac{\partial \Delta H}{\partial P}\right)_{x,T}\left(\frac{\partial P}{\partial x}\right)_{\Delta V,T}$$

$$\left(\frac{\partial P}{\partial x}\right)_{\Delta V,T} = -\left(\frac{\partial \Delta V}{\partial x}\right)_{P,T} \Big/ \left(\frac{\partial \Delta V}{\partial P}\right)_{x,T}$$

whence

$$\left(\frac{\partial \Delta H}{\partial x}\right)_{P,T} = \left(\frac{\partial \Delta H}{\partial x}\right)_{\Delta V,T} + \left(\frac{\partial \Delta H}{\partial P}\right)_{x,T}\left(\frac{\partial \Delta V}{\partial x}\right)_{P,T} \Big/ \left(\frac{\partial \Delta V}{\partial P}\right)_{x,T} \quad . \quad . \quad (12)$$

It was suggested [1] that $(\partial \Delta H/\partial x)_{\Delta V,T}$ may be neglected if ΔH is proportional to ΔV at a given pressure and temperature. This condition is necessary but not sufficient. Let $\Delta H(P,T,x) = A(P,T) \,.\, \Delta V(P,T,x)$ where A is a constant of proportionality that is independent of x at a given P and T. Then

$$\left(\frac{\partial \Delta H}{\partial x}\right)_{\Delta V,T} = \Delta V \left(\frac{\partial A}{\partial x}\right)_{\Delta V,T}$$

$$= -\Delta V \left(\frac{\partial A}{\partial P}\right)_{T}\left(\frac{\partial \Delta V}{\partial x}\right)_{P,T} \Big/ \left(\frac{\partial \Delta V}{\partial p}\right)_{x,T}$$

This is zero only if A is independent of pressure. In general A is a function of pressure, and is certainly so for the statistical models cited,[1] for which this term in eqn. (12) is the larger and is of opposite sign to the term retained. Any value of this equation without this term must therefore be justified experimentally.

Since either ΔV or $T(\partial \Delta V/\partial T)_{P,x}$ may be the greater, Mathieson's eqn. (15) allows ΔH to be positive or negative for positive ΔV, as is required.

However, for the system cyclohexane–carbon tetrachloride the sign of

$$(\partial P/\partial \Delta V)_{T,x}(\partial \Delta H/\partial P)_{T,x}$$

has been overlooked and the apparent agreement for this system is fortuitous.[1] For the other three non-polar systems considered,[1] $T(\partial \Delta V/\partial T)_{P,x} > \Delta V$ and the agreement stands. The disagreement for cyclohexane–carbon tetrachloride may be connected with the unusual variation [2] of $(\partial \Delta V/\partial T)_{P,x}$ with x. For the other systems, even ethanol–water, this has a maximum value at some intermediate value of x around 0·5, but for cyclohexane–carbon tetrachloride it is roughly linear in x, passing through zero at about $x = 0{\cdot}6$. Further experimental evidence exists in favour of eqn. (12), with $(\partial \Delta H/\partial x)_{\Delta V,T}$ neglected. Scatchard [3] has derived equations $(\Delta E)_V = \Delta V/\beta$ and

$$(\Delta H)_P = (\Delta V/\beta)[1 + T(\partial V/\partial T)/V - \Delta V\,(1 + \mathrm{d} \ln \beta/\mathrm{d}T)/2V]$$

which closely resemble Mathieson's eqn. (15) when $\beta = \beta_0$, and they have been tested by Meares [4] who found good agreement for a wide range of mixtures of butane-1,3-diol diacetate with other esters.

No general relation between ΔH and ΔV has been sought from classical thermodynamics, as restrictive conditions have been imposed,[1] the validity of which can only be determined by comparison with experiment.

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[1] Wood and Gray, *J. Amer. Chem. Soc.*, 1952, **74**, 3729.
[2] Scatchard, *Trans. Faraday Soc.*, 1937, **33**, 160.
[4] Meares, *ibid.*, 1949, **45**, 1066.

833. *Chlorine Hydrate.*

By K. W. Allen.

Chlorine hydrate has a formula $Cl_2,7{\cdot}27 \pm 0{\cdot}17H_2O$.

Chlorine hydrate has been investigated often since Davey deduced that it is a compound.[1] Faraday analysed it and concluded that it should be represented as $Cl_2,10H_2O$.[2] Roozeboom [3] determined the saturated vapour pressure–temperature relationships from $-10°$ to $+16°$ and carried out a series of analyses from which he concluded that the formula was $Cl_2,8H_2O$. Much recent work has used Roozeboom's results. Further analyses have been reported by Bouzat and Azinieres [4] and Anwar-Ullah [5] all of which led to the formula $Cl_2,6H_2O$.

There have been several thermodynamic discussions, all using essentially a Hess's law type of calculation. Of these, the most significant [6] concludes that the formula should be $Cl_2,8H_2O$, but this depends entirely upon Roozeboom's data.[3]

More recently, consideration of clathrate compounds has led to a fuller understanding of the gas hydrates and particularly of chlorine hydrate. They are now explained as a regular framework of water molecules containing voids or holes large enough to contain gas molecules. Two separate structures have been described to account for gas hydrates (*e.g.*, chlorine, sulphur dioxide, methyl chloride) with a cell-constant of 12 Å, and the liquid hydrates (*e.g.*, ethyl chloride, chloroform) with a cell-constant of 17·2 Å. Each of these contains holes of two different sizes. The unit cell of the gas hydrate structure contains 46 water molecules and provides two small and six medium holes, while that of the liquid hydrate contains 136 water molecules and provides sixteen small and eight large holes.[7,8] For a particular gas hydrate, depending largely upon the size of the gas molecule, there are four possibilities: medium holes all filled; medium and small holes all filled; all medium and some small holes filled; some medium and some small holes filled.

For chlorine hydrate, von Stackelberg *et al.*[8] assumed a formula $Cl_2,6H_2O$ and explained this as due to a 96% filling of all the holes. Pauling and Marsh [9] compared the *X*-ray diffraction patterns measured for chlorine hydrate with those calculated for the general gas-hydrate structure, assuming different ways of filling the holes. They deduced that chlorine molecules occupy the medium holes only and none of the small holes, and consequently they predicted a composition corresponding to $Cl_2,7\frac{2}{3}H_2O$.

Further understanding of this compound depends upon a precise knowledge of its actual composition, which we have now established.

The value $7{\cdot}27 \pm 0{\cdot}17$ found for the ratio of water to chlorine molecules does not correspond exactly to the filling of the medium holes as suggested by Pauling and Marsh,[9] for which the value is 7·67. It is even further from the value 6·0 used by von Stackelberg [8] which approximates to filling all medium and small holes.

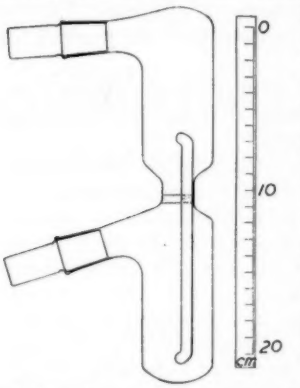
In view of Pauling and Marsh's results,[9] it seems certain that the structure involves filling of all the medium holes together with a few of the small holes with chlorine molecules. If 20% of the small holes are filled, a structure and composition consistent with the experimental result is obtained. This proposition is further supported by the calculated value for the density which is 1·29 g./ml. for this structure (1·26 g./ml. for $6Cl_2,46H_2O$; 1·40 g./ml. for $8Cl_2,46H_2O$; 1·38 g./ml. for $Cl_2,6H_2O$). The experimental value, reported by von Stackelberg *et al.*,[8] is $1{\cdot}29 \pm 0{\cdot}02$ g./ml.

[1] Davey, *Phil. Trans.*, 1811, **101**, 30.
[2] Faraday, *Quart. J. Science, Literature, and Arts*, 1823, **15**, 71.
[3] Roozeboom, *Rec. Trav. chim.*, 1884, **3**, 59; 1885, **4**, 65.
[4] Bouzat and Azinieres, *Bull. Soc. chim. France*, 1924, **35**, 545.
[5] Anwar-Ullah, *J.*, 1932, 1172.
[6] Ivan Harris, *Nature*, 1943, **151**, 309.
[7] Clausen, *J. Chem. Phys.*, 1951, **19**, 259, 662, 1425.
[8] von Stackelberg *et al.*, *Z. Electrochem.*, 1954, **58**, 25, 40, 99, 104, 162.
[9] Pauling and Marsh, *Proc. Nat. Acad. Sci. U.S.A.*, 1952, **38**, 112.

XUM

Experimental

To avoid having to dry the crystals of chlorine hydrate, which had been a source of constant difficulty and error in all previous analytical work, Schreinmakers' wet-residue method was used.[10] Chlorine hydrate was prepared by passing a stream of chlorine gas at atmospheric pressure through dilute solutions of calcium chloride (5—14% of $CaCl_2$) at 0°. Because the crystals are very feathery and difficult to separate adequately from the mother-liquor, this was done in a special equilibrium apparatus which consisted of two glass bulbs separated by a coarse sintered-glass disc (Figure). Chlorine was passed in through the upper opening. It went through the side tube and bubbled up through the solution. Excess of gas escaped from the lower opening to waste. When a fair quantity of solid hydrate had formed, the openings were closed with glass-stoppers lubricated with " Fluorube " grease. The whole apparatus was kept in ice for several days, with occasional shaking to attain equilibrium, then inverted so that the solid was filtered off on the sintered disc, and left inverted in ice for several hours to allow the solid to drain. Portions of the solid were transferred with a dry fork made of very fine glass rod to tared weighing bottles containing saturated potassium iodide solution. Samples of the liquid were transferred with an all-glass hypodermic syringe fitted with a glass needle to similar weighing bottles. From this stage all the samples were analysed in the same way. After re-weighing, the samples were transferred to beakers and the iodine which had been liberated by the free chlorine was titrated with 0·05N-sodium thiosulphate and sodium starch glycollate indicator. Then the calcium chloride was determined gravimetrically in these solutions by precipitation as calcium oxalate, ignition to calcium carbonate, and weighing.



Since in each case the wet solid of known total composition is a mixture of liquid of known composition and dry solid, the composition of the dry solid can be found. Usually this is done by graphical extrapolation on an equilateral triangle, but in this instance the intersections were too acute for this method to be sufficiently accurate. The results were plotted on rectangular co-ordinates and the extrapolations were all calculated algebraically.

Sixteen conjugate pairs of liquid and wet solid were analysed and the compositions of dry solids were calculated. The final value for the composition of chlorine hydrate was 35·15 ± 0·54% of chlorine. This corresponds to a formula $Cl_2,7{\cdot}27 \pm 0{\cdot}17H_2O$.

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London, E.C.1. [*Received, June 3rd,* 1959.]

[10] Schreinmakers, *Z. phys. Chem.*, 1893, **11**, 75.

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834. *The Ionisation Potential of* NH.

By R. I. Reed and W. Snedden.

The latent heat of the sublimation of carbon and the heat of atomisation of nitrogen are not independent quantities [1] and the preferred value [2] of $L(C) = 7{\cdot}386$ ev leads to $D(N{-}N) = 9{\cdot}67$.[3] It is accordingly of interest to examine, by electron-impact methods already described,[2] certain of the bond-dissociation energies in ammonia. The experimental results, which are more extensive than those hitherto obtained are in the Table.

[1] Cottrell, " The Strengths of Chemical Bonds," Butterworths, London, 1954, p. 165.
[2] Reed and Snedden, *Trans. Faraday Soc.*, 1958, **54**, 949.
[3] Franklin and Field, " Electron Impact Phenomena and the Properties of Gaseous Ions," Academic Press Inc., New York, 1957, p. 270.

It appears that Mann, Hustrulid, and Tate's [4] earlier method has yielded an average value for $A(^{+}NH)$ and only the excited states of the nitrogen ion for $A(^{+}N)$.

Species	NH	N
Appearance potential (ev ± 0·1)	17·1, 21·6	22·6, 24·1, 26·65, 28·6
,, ,, (ev ± 0·5, ref. 4)	19·4	25·0, 28·1
Ionisation potential (ev ± 0·05)	13·10	—

There is already good evidence for the value of the first bond-dissociation energy obtained by electron-impact studies upon ammonia,[4] and also by the pyrolysis of hydrazine [5] and benzylamine,[6] the values being 4·50 ev, 4·34 ev, and 4·51 ± 0·08 ev respectively—in good agreement.

Our work has shown two appearance potentials for the ^{+}NH ion 4·5 ± 0·2 ev apart. Such a difference, which corresponds to the dissociation energy of molecular hydrogen, suggests that this ion is obtained by the two reaction processes:

$$e + NH_3 \longrightarrow {}^{+}NH + H_2 + 2e \quad \ldots\ldots\ldots (1)$$

$$e + NH_3 \longrightarrow {}^{+}NH + 2H + 2e \quad \ldots\ldots\ldots (2)$$

the second being associated with the value of 21·6 ± 0·1 ev.

The available test for the presence of excess of kinetic energy [2] suggests that it is absent, and, the production of all the fragments in their electronic ground states being assumed, $D(NH\text{–}H) = A(^{+}NH) - I(NH) - D(NH_2\text{–}H) + D(H\text{–}H)$ can be written for eqn. (1), and the same expression less the final term $D(H\text{–}H)$ for (2). Substituting the measured values and $D(NH_2\text{–}H) = 4{\cdot}50$ ev, we obtain the energy 4·0 ± 0·15 ev in each case.

A similar examination of the appearance potentials of the N^{+} ion from ammonia gave four values which are considered to result from two fragmentations:

$$e + NH_3 \longrightarrow N^{+} + H_2 + H + 2e \quad \ldots\ldots\ldots (3)$$

$$e + NH_3 \longrightarrow N^{+} + 3H + 2e \quad \ldots\ldots\ldots (4)$$

in which all the fragments are formed in their electronic ground states, and two in which the N^{+} ion is formed in the ^{1}D state. These considerations lead to four equations for $D(N\text{–}H)$ of which

$$D(N\text{–}H) = A(N^{+}) = I(N) - D(NH_2\text{–}H) - D(NH\text{–}H) + D(H\text{–}H)$$

and

$$D(N\text{–}H) = A(^{*}N^{+}) - I(N) - D(NH_2\text{–}H) - D(NH\text{–}H) + e$$

are two, $^{*}N^{+}$ representing the electronically excited nitrogen ion. Substitution of the previously determined bond energies and the spectroscopic quantities $I(N) = 14{\cdot}477$ ev [7] and $E_e = N^{+}(^{3}P) \longrightarrow N^{+}(^{1}D) = 1{\cdot}90$ ev [8] gives $D(N\text{–}H) = 3{\cdot}7 \pm 0{\cdot}25$ ev, 3·67 ± 0·25 ev, 3·7 ± 0·25 ev, and 3·7 ± 0·25 ev. A spectroscopic determination of $D(N\text{–}H) = 3{\cdot}8$ ev [8] has already been made, and the present values are in good agreement. This quantity together with the heats of atomisation of nitrogen and hydrogen allow the evaluation of $\Delta H_f(NH, g) = 3{\cdot}57$ ev, a figure previously obtained by Altshuller.[9] Combining this quantity with $\Delta H_f(NH_2, g) = 1{\cdot}76$ ev, we obtain the bond-dissociation energy $D(NH\text{–}H) = 4{\cdot}07$ ev. This agrees well with the present electron-impact value, suggesting that $I(NH) = 13{\cdot}10 \pm 0{\cdot}05$ ev is probably correct. The ionisation potentials of the isoelectronic species are $I(O) = 13{\cdot}61$ ev [10] and $I(CH_2) = 11{\cdot}9 \pm 0{\cdot}1$ ev.[11]

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[4] Mann, Hustrulid, and Tate, *Phys. Rev.*, 1940, **58**, 340.
[5] Szwarc, *Proc. Roy. Soc.*, 1949, *A*, **198**, 267.
[6] *Idem, ibid.*, p. 285.
[7] Moore, Nat. Bur. Stand. Circular No. 467, 1949.
[8] Pannetier and Gaydon, *J. Chim. phys.*, 1951, **48**, 221.
[9] Altshuller, *J. Chem. Phys.*, 1954, **22**, 1947.
[10] Nier and Hanson, *Phys. Rev.*, 1936, **50**, 722.
[11] Langer, Hipple, and Stevenson, *J. Chem. Phys.*, 1954, **22**, 1836.

XUM

835. *Hydrolysis of Isopropylideneglycerol Esters of Fatty Acids.*

By L. Hartman.

For the preparation of pure α-monoglycerides of fatty acids the classical method of Fischer *et al.*[1] based on the acylation of isopropylideneglycerol is regarded as most reliable and convenient.[2] The only difficulty is encountered in the removal of the blocking group, which is accomplished by hydrolysis with mineral acids. This hydrolysis requires varying conditions depending on the molecular weight of the fatty acids and induces partial splitting of the low-molecular monoglycerides into glycerol and fatty acids. Some isomerisation to β-monoglycerides also appears possible in view of recent findings [3] that there exists an equilibrium between the 1- and the 2-ester, involving 8—10% of the latter. Aqueous acetic acid [4] is well suited for the hydrolysis of isopropylideneglycerol esters of C_2—C_5 acids, but the hydrolysis becomes increasingly difficult with the homologous acids, and impracticable from nonanoic acid onward. Boric acid, used successfully by Martin [5] in the removal of the benzylidene group from 2-acyl-1,3-benzylideneglycerols, was found in the present work to be a convenient reagent in the hydrolysis of isopropylideneglycerol esters. This acid is known to form esters with glycerol which are readily decomposed on contact with water. Thus cleavage of isopropylideneglycerol esters with boric acid, followed by treatment with water, leads to α-monoglycerides. The main difficulty was the selection of a suitable co-solvent for boric acid and the esters. Triethyl borate used by Martin [5] is difficult to prepare and, moreover, was not particularly effective in this instance. Dioxan, several alcohols, and other solvents were tried with varying success and finally 2-methoxyethanol was selected as most convenient. Contrary to expectation the hydrolysis with boric acid and hydrochloric acid produced similar amounts of impurities in the case of high-molecular esters, and no saving in the purification of the crude product could be achieved. Nevertheless, the procedure described below may be found a convenient alternative to the classical method because of the greater ease of operation, particularly for esters of acids of medium chain length (C_8—C_{12}), the hydrolysis of which requires otherwise special precautions. Monocaproin represents about the limit of the usefulness of the proposed procedure. Monoglycerides of C_2—C_5 acids, which are increasingly soluble in water, are best prepared by hydrolysis with aqueous acetic acid.[4]

Experimental.—Isopropylideneglyerol esters of highly purified fatty acids were prepared by the classical method as modified by Daubert *et al.*[6] After the evaporation of solvents used they were dried in a vacuum-desiccator, and aliquot parts were hydrolysed to monoglycerides. A few examples are given below.

α-*Monostearin.* Isopropylideneglycerol stearate (4 g., 0·01 mole) and finely powdered boric acid (6·2 g., 0·1 mole) were heated with 2-methoxyethanol (20 ml.) on a boiling-water bath for 30 min. A small amount of boric acid remained undissolved. The mixture was taken up in ether and washed three times with water, the ethereal solution was dried (Na_2SO_4), most of the solvent was evaporated, and the product was dried first in the air and finally in a vacuum-desiccator. The yield of crude monoglyceride was 3·6 g. (theoretical); it had m. p. 78—79°, acid value 4·7, and α-monoglyceride content by the periodate method [7] 89·8%. After two crystallisations from ether pure α-monostearin, m. p. 81—81·5°, was obtained. Crude monostearin prepared by hydrolysis with hydrochloric acid had m. p. 79—80°, acid value 2·8, and α-monoglyceride content 91·3%. Determination of β-monoglycerides in both crude products by the method of Brokaw *et al.*[8] gave no definite results since perchloric acid used as the isomeris-

[1] Fischer, Bergmann, and Bärwind, *Ber.*, 1920, **53**, 1589.
[2] Malkin and Bevan, in "Progress in the Chemistry of Fats and Other Lipids," Pergamon Press, London, 1957, Vol. IV, p. 66.
[3] Martin, *J. Amer. Chem. Soc.*, 1953, **75**, 5483.
[4] Baer and Fischer, *ibid.*, 1945, **67**, 2031.
[5] Martin, *ibid.*, 1953, **75**, 5482.
[6] Daubert, Fricke, and Longenecker, *ibid.*, 1943, **65**, 2142.
[7] Pohle and Mehlenbacher, *J. Amer. Oil Chemists' Soc.*, 1950, **27**, 54.
[8] Brokaw, Perry, and Lyman, *ibid.*, 1955, **32**, 194.

ation reagent hydrolysed some of the residual isopropylideneglycerol ester. It seems, however, that neither product contained appreciable amounts of the β-isomer.

In practice drying of isopropylideneglycerol ester and isolation of the crude monoglyceride can be omitted.

α-Monolaurin. Crude monolaurin prepared in 97% yield by using similar molar proportions and conditions had m. p. of 58—59°, acid value 8·4, and α-monoglyceride content 87·7%. After crystallisation from a mixture of ether and light petroleum the m. p. rose to 62—63°.

α-Monocaprylin. The crude product had m. p. of 34·5—35·8°, acid value 12·2, and α-monoglyceride content 87·6%. After several crystallisations from light petroleum the m. p. was 39·5—40·5° and the α-monoglyceride content 100·9%. (No m. p. for racemic α-monocaprylin could be found in the literature. The m. p. of the optically active L-α-monoglyceride had been reported as 28—30°.[4])

α-Monocaproin. Isopropylideneglycerol hexanoate (4·6 g., 0·02 mole), boric acid (6·2 g., 0·1 mole), and 2-methoxyethanol (20 ml.) were heated at 100° for 30 min. The mixture was taken up in 5% aqueous sodium hydrogen carbonate and extracted three times with ether. The syrup remaining after evaporation of the ether was purified by extraction with light petroleum in which the monoglyceride is difficultly soluble. After a final crystallisation from ether–light petroleum (1 : 3) at −20° the m. p. was 18·5—19·5° (lit.,[9] 19·4°) and the α-monoglyceride content 99·4%.

Thanks are expressed to Miss J. M. Monnie for technical assistance.

FATS RESEARCH LABORATORY, DEPARTMENT OF SCIENTIFIC AND INDUSTRIAL RESEARCH, WELLINGTON, NEW ZEALAND. [*Received, June 22nd*, 1959.]

[9] Daubert, Spiegl, and Longenecker, *J. Amer. Chem. Soc.*, 1943, **65**, 2144.

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836. *A Deuterium Isotope Effect in the Oxidation of Cyclohexanol by Cerium*(IV).

By J. S. LITTLER.

THERE is a primary kinetic isotope effect in the oxidation of cyclohexanol and 1-deuterocyclohexanol by quinquevalent vanadium in acid solutions.[1] As the existence of such an effect in the oxidation of an alcohol by another one-electron oxidant had not been observed, the oxidation of the above alcohols by ceric sulphate has now been studied. A kinetic isotope effect $k_H/k_D = 1·9$ has been found, indicating that this reaction also proceeds by a mechanism that requires participation of the C–H bond in the rate-determining process.

Ardon,[2] who studied the oxidation of ethanol by cerium(IV) in perchloric acid, deduced a rate equation

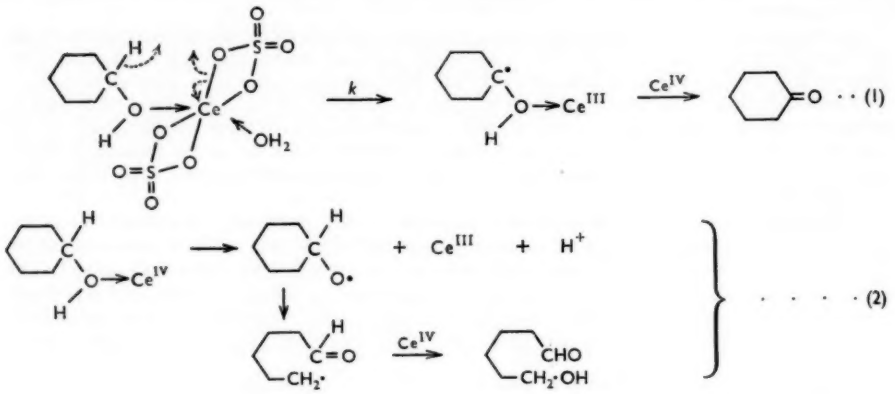
$$\frac{d[Ce^{IV}]}{dt} = \frac{kK[Ce^{IV}][\text{alcohol}]}{1 + K[\text{alcohol}]}$$

indicating that a Ce^{IV}–alcohol complex is formed with a stability constant $K = 4·3$ and a decomposition rate constant $k = 67 \times 10^{-4}$ sec.$^{-1}$ at 20°. Our results fit a similar equation in which $K = 13·0$ and $k = 1·38 \times 10^{-4}$ sec.$^{-1}$ at 50°. Here K is the apparent constant based on the total concentration of cerium(IV), though in fact several ceric sulphate complexes may be reacting species.[3,4]

As in the case of the oxidation by vanadium, the existence of the isotope effect indicates that the oxidation step probably involves one-electron transfers within a cyclic alcohol–Ce^{IV} complex as in eqn. (1), but the low value of k_H/k_D (cf. $k_H/k_D = 3·6$ for V^V in $HClO_4$ and 4·5 in H_2SO_4) shows the possibility of concurrent oxidation by an acyclic mechanism such

[1] Littler and Waters, *J.*, 1959, 4046.
[2] Ardon, *J.*, 1957, 1811.
[3] Hardwick and Robertson, *Canad. J. Chem.*, 1951, **29**, 828.
[4] Mino, Kaiserman, and Rasmussen, *J. Amer. Chem. Soc.*, 1959, **81**, 1494.

as (2), corresponding to that suggested by Bawn and White [5] for the oxidation of alcohols by the much more vigorous oxidant cobalt(III).



Results.—The kinetic measurements were made titrimetrically as in ref. 1. k is the first-order constant, calculated from initial rates of oxidation; the initial organic products are

Oxidation of cyclohexanol and 1-deuterocyclohexanol by Ce^{IV} *at 50°.*

$[H_2SO_4] = 0{\cdot}24$M; $[Ce^{IV}] = 0{\cdot}0218$N.

	Cyclohexanol				1-Deutero-cyclohexanol
[Alcohol]	0·3054	0·2036	0·1018	0·0160	0·0826
10^4k (sec.$^{-1}$)	1·085	1·005	0·78	0·605	0·382

further oxidised and accelerate the reduction of Ce^{IV}, but this was expected.[2] If $1/k$ is plotted against 1/[alcohol] for the H-alcohol, a good straight line is obtained, showing Ardon's equation to be valid. The point for the D-alcohol is well away from the curve, showing its slower oxidation.

I thank Dr. W. A. Waters, F.R.S., for his interest and encouragement and the Salters' Company for a Scholarship.

DYSON PERRINS LABORATORY, OXFORD. [*Received, June 22nd,* 1959.]

[5] Bawn and White, *J.*, 1951, 343.

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837. *Aspects of Stereochemistry. Part XIV.* Addition of Hypobromous Acid to* Δ^1*-Steroids.*

By H. B. HENBEST and R. A. L. WILSON.

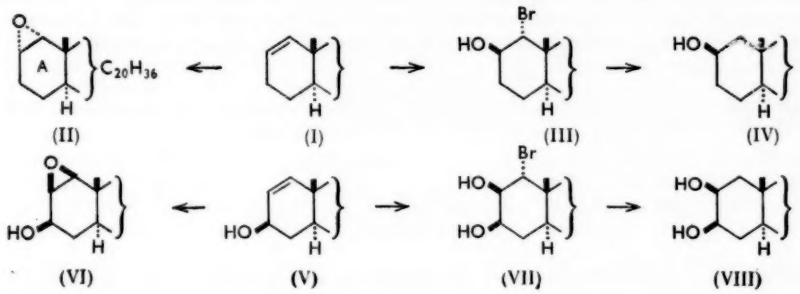
THE reactions of 5α-cholest-1-ene (I) and 5α-cholest-1-en-3β-ol (V) with peracids give respectively the α-epoxide (II) by normal rear attack and the β-epoxide (V).[1,2] The unusual course of the latter reaction has been discussed, the suggestion being made that hydrogen-bonding occurs between the 3β-hydroxyl group of the steroid and the peracid molecule during the reaction.[2]

* Part XIII, Henbest and McElhinney, *J.*, 1959, 1834.

[1] Henbest and Wilson, *J.*, 1956, 3289.
[2] *Idem, J.*, 1957, 1958.

It was of interest to find out if other electrophilic reagents might also add to the double bond of the allylic alcohol (V) in an unusual fashion. Additions of hypobromous acid to the compounds (I and V) are now reported, the reactions being carried out in aqueous t-butyl alcohol containing *N*-bromosuccinimide and perchloric acid.

One bromohydrin (75% yield) was obtained from the parent 5α-cholest-1-ene (I). Its structure (III) was established by reduction with sodium and ammonia to the known 2β-alcohol (IV). The formation of the bromohydrin (III) presumably occurs *via* a 1α,2α-bromonium ion that opens to the diaxial product on reaction with water.



Reaction of the allylic alcohol (V) under the same conditions gave 5α-cholest-1-en-3-one (36%) and a bromohydrin (60%), whose structure (VII) was proved by reduction to the known 2β,3β-diol (VIII). The ketone and bromohydrin were separated by chromatography on neutral alumina; use of alkaline alumina gave 1β,2β-epoxycholestan-3β-ol (VI) instead of the bromohydrin. The formation of the bromohydrin (VII) from the allylic 3β-alcohol (V) is best explained as proceeding through a 1α,2α-bromonium ion. The course of the reaction provides no evidence for the intermediate production of a 1β,2β-bromonium ion, analogous to the formation of the 1β,2β-epoxide (VI), as this would have led to a 2β-bromo-1α,3β-diol.

Experimental.—M. p.s were determined on a Kofler block. Rotations were measured for chloroform solutions. P. Spence alumina (Grade H) was used for chromatography; dilute acetic acid was used to neutralize and deactivate the alumina.[3]

1α-*Bromo*-5α-*cholestan*-2β-*ol* (III). *N*-Bromosuccinimide (50 mg.) in aqueous t-butyl alcohol (30 c.c.; 5% of water), and N-perchloric acid (0·5 c.c.), were added in succession to a solution of 5α-cholest-1-ene (0·1 g.) in aqueous t-butyl alcohol (20 c.c.) at 0°. The solution was kept at 0° for 16 hr. The steroid was then isolated with ether. **1α-*Bromo*-5α-*cholestan*-2β-*ol*** (95 mg.) was obtained as needles, m. p. 113—116° (from acetone), $[\alpha]_D$ +40° (Found: C, 69·5; H, 10·3. $C_{27}H_{47}OBr$ requires C, 69·35; H, 10·1%).

The bromohydrin (50 mg.), in ether (30 c.c.) and methanol (1 c.c.), was added dropwise to a stirred solution of sodium (0·2 g.) in liquid ammonia (50 c.c.) and ether (30 c.c.). After an hour the steroid was isolated with ether. Crystallization from acetone gave 5α-cholestan-2β-ol (20 mg.), m. p. and mixed m. p. 151—154°, $[\alpha]_D$ +35°.

1α-*Bromo*-5α-*cholestane*-2β,3β-*diol* (VII). Solutions of 5α-cholest-1-en-3β-ol (1 g.) in aqueous t-butyl alcohol (50 c.c.; 5% of water), and *N*-bromosuccinimide (0·5 g.) in aqueous t-butyl alcohol (30 c.c.; 5% of water), were mixed at 0° and N-perchloric acid (2 c.c.) was added. The solution was kept at 0° for 16 hr. The steroid was then isolated with ether. Chromatography on neutral, deactivated alumina (100 g.) gave cholest-1-en-3-one (0·36 g.) (eluted with benzene, 200 c.c.), m. p. and mixed m. p. 97—99°, and **1α-*bromo*-5α-*cholestane*-2β,3β-*diol*** (0·76 g.) (eluted with 700 c.c. of 9 : 1 benzene–ether), m. p. 186—188° [from light petroleum (b. p. 60—80°)], $[\alpha]_D$ +35° (Found: C, 66·7; H, 9·8%. $C_{27}H_{47}O_2Br$ requires C, 67·05; H, 9·8%).

In another experiment, the product was chromatographed on normal alumina (100 g.).

[3] Farrar, Hamlet, Henbest, and Jones, *J.*, 1952, 2657.

XUM

Elution with benzene (400 c.c.) gave 5α-cholest-1-en-3-one (0·31 g.), m. p. and mixed m. p. 97—100°; elution with ether (500 c.c.) gave 1β,2β-epoxy-5α-cholestan-3β-ol (VI) (0·5 g.), m. p. and mixed m. p. 173—176° (from acetone) (Found: C, 80·4; H, 10·6. Calc. for $C_{27}H_{46}O_2$: C, 80·6; H, 11·5%).

The bromo-diol (0·2 g.) in ether (50 c.c.) and methanol (1 c.c.) was added slowly to a stirred solution of sodium (0·5 g.) in liquid ammonia (1 l.) and ether (30 c.c.). After 1·5 hr., the steroid was isolated with ether. Crystallization from acetone gave 5α-cholestane-2β,3β-diol (VIII) (0·1 g.), m. p. and mixed m. p. 173—176°, $[\alpha]_D$ +30°.

1β,2β-*Epoxy-5α-cholestan-3β-yl Methanesulphonate.* Methanesulphonyl chloride (0·6 c.c.) was added to a solution of 1β,2β-epoxy-5α-cholestan-3β-ol (0·7 g.) in pyridine at 0°. The mixture was kept at 20° for 16 hr., then the *ester* was isolated with ether. It (0·7 g.) had m. p. 133—136° (from methanol), $[\alpha]_D$ +176° (Found: C, 70·0; H, 10·1. $C_{28}H_{48}O_4S$ requires C, 69·95; H, 10·05%).

We thank the Department of Scientific and Industrial Research for financial assistance (to R. A. L. W.) and Messrs. E. S. Morton and H. Swift for analyses.

THE UNIVERSITY, MANCHESTER, 13.
THE QUEEN'S UNIVERSITY OF BELFAST. [*Received, June 22nd,* 1959.]

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838. *Rapid, Simple, and Inexpensive Preparation of* [$^2H_3$]*Methyl Iodide and* [$^2H_6$]*Dimethyl Sulphoxide.*

By F. A. COTTON, J. H. FASSNACHT, W. D. HORROCKS, jun., and N. A. NELSON.

FULLY deuterated methyl iodide and dimethyl sulphoxide, especially the former, are useful. The former is a common starting material in the preparation of compounds containing [$^2H_3$]methyl groups; the latter is an unusually good solvent for most classes of organic compound except aliphatic hydrocarbons, and for use in proton magnetic resonance spectroscopy.[1] Its usefulness would be enhanced by ready availability and cheapness. The usual method of preparing [$^2H_3$]methyl iodide involves four steps, *viz.*, (1) deuteration of malonic acid followed by (2) decarboxylation to yield [$^2H_4$]acetic acid, then (3) conversion of this into the silver salt and (4) Hunsdiecker decarboxylation by heating with iodine. We have been unable to find any method in the literature for the preparation of the sulphoxide.

This note describes a quicker, more convenient, and therefore cheaper method of preparing [$^2H_3$]methyl iodide, yielding also [$^2H_6$]dimethyl sulphoxide. The method was suggested by Kuhn and Trischmann's observation [2] that trimethyloxosulphonium iodide ($Me_3S^+O\ I^-$), easily made by addition of methyl iodide to dimethyl sulphoxide, could be pyrolysed smoothly back to these substances, and Smith and Winstein's observation [3] that trimethyloxosulphonium nitrate readily exchanges with neutral deuterium oxide. Actually, we find that exchange between the iodide and water occurs rapidly only in slightly basic solution. Our reactions are thus:

$$(CH_3)_2SO + CH_3I = (CH_3)_3S^+OI^- \quad (1)$$

$$(CH_3)_3S^+O + D_2O\ (\text{excess}) = (CD_3)_3S^+O + H_2O \quad (2)$$

$$(CD_3)_3S^+OI^- \longrightarrow CD_3I + (CD_3)_2SO\ \text{by pyrolysis} \quad (3)$$

If only the methyl iodide is required, the sulphoxide can be recycled.

A sequence of the same type will probably yield [1,1-$^2H_2$]ethyl iodide from which various [1,1-$^2H_2$]ethyl derivatives, some possibly of use in structural determinations by microwave spectroscopy, may be obtained.

[1] Slomp and McGarvey, *J. Amer. Chem. Soc.*, 1959, **81**, 2200; also unpublished work in this laboratory.
[2] Kuhn and Trischman, *Annalen*, 1958, **611**, 117.
[3] Smith and Winstein, *Tetrahedron*, 1958, **3**, 317.

Experimental.—[$^2H_9$]*Trimethyloxosulphonium iodide.* Trimethyloxosulphonium iodide [2] (38 g.) was dissolved in 170 ml. of 99·5% deuterium oxide at 80—100°, and 50 mg. of anhydrous potassium carbonate were added. The solution was heated on a steam-bath for 1 hr., then cooled to 0° for at least 2 hr. before the precipitate was filtered off. The solid was equilibrated twice more by the same procedure to give 33·4 g. (88%) of product.

[$^2H_3$]*Methyl iodide and* [$^2H_6$]*dimethyl sulphoxide.* In a small pear-shaped flask connected through a short Vigreux column to an ice-cooled trap and a liquid-nitrogen trap in series, the whole being connected to a water aspirator through a drying tower, 33·4 g. of [$^2H_9$]trimethyloxosulphonium iodide was heated to 200°/20 mm. After 2 hr., during which a small amount of liquid distilled, the crystalline mass melted and rapidly decomposed. Distillation of the material in the first receiver gave 8·9 g. of crude [$^2H_3$]methyl iodide (collected at atmospheric pressure) and 9·45 g. (80%) of [$^2H_6$]dimethyl sulphoxide, b. p. 88°/24 mm. The yellow colour which frequently forms in the latter liquid can be removed by gentle warming with a little solid sodium thiosulphate followed by distillation from barium oxide. The crude [$^2H_3$]methyl iodide and the material in the liquid nitrogen-cooled trap were combined and distilled, giving 17·6 g. (84%) of [$^2H_3$]methyl iodide, b. p. 41°.

Both products had 99·0—99·2% deuteration.

This work was supported in part by the U.S. Atomic Energy Commission. We thank Professor K. Biemann and Dr. J. Seibl for mass-spectrographic analyses.

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[*Received, June 30th*, 1959.]

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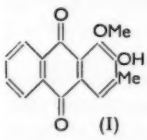
839. *Naturally Occurring Quinones. Part III.* A Synthesis of Digitolutein.*

By J. C. Lovie and R. H. Thomson.

Digitolutein is a yellow pigment found in the leaves of the foxgloves, *Digitalis lutea* Linn.[1] and *D. purpurea* Linn.[2] Degradative studies by Janot *et al.*[3] established that the structure was 3-methylalizarin 1-methyl ether (I), and we have now confirmed this by synthesis.

3-Methylalizarin has previously been obtained from 2-hydroxy-3-methylanthraquinone (itself obtained by a two-step condensation of *o*-cresol and phthalic anhydride) by direct,[4] or indirect,[3,5] hydroxylation. We find 3-methylalizarin can be conveniently synthesised on a small scale in one step by condensation of 3-methylcatechol with phthalic anhydride in fused aluminium chloride–sodium chloride. Sublimation of the crude product gives 3-methylalizarin adequate for further synthesis. Acetylation in the presence of boroacetic anhydride afforded 3-methylalizarin 2-acetate which was converted, by methylation and subsequent hydrolysis, into 3-methylalizarin 1-methyl ether, identical with natural digitolutein.



(I)

An attempt to synthesise 1,2,6,8-tetrahydroxy-3-methylanthraquinone, one of the pigments of *Rhamnus alaternus* Linn.,[6] by a similar condensation of 3-methylcatechol with 3,5-dimethoxyphthalic anhydride failed. Interaction of these compounds under normal Friedel–Crafts conditions was also unsuccessful owing to the instability of the anhydride which was decarboxylated to 3,5-dimethoxybenzoic acid.

* The papers, *J.*, 1949, 1277 and 1951, 1237, are regarded as Parts I and II of this series.

[1] Adrian and Trillat, *Compt. rend.*, 1899, **129**, 889.
[2] Paris, *Compt. rend.*, 1954, **238**, 932.
[3] Janot, Chabasse-Massonneau, de Graeve, and Goutarel, *Bull. Soc. chim. France*, 1955, 108.
[4] Mitter and Sen, *J. Indian Chem. Soc.*, 1928, **5**, 631.
[5] Mitter and Pal, *J. Indian Chem. Soc.*, 1930, **7**, 259.
[6] Briggs, Jacombs, and Nicholls, *J.*, 1953, 3069.

XUM

Experimental.—*3-Methylalizarin.* An intimate mixture of 3-methylcatechol (2·5 g.) and phthalic anhydride (3 g.) was stirred into a molten mixture of anhydrous aluminium chloride (50 g.) and sodium chloride (10 g.) at 120°. The temperature was raised rapidly to 180—200°, and kept there for 5—10 min. with continuous stirring. After some cooling, the melt was poured on ice (500 g.) and concentrated hydrochloric acid (500 ml.). The brown precipitate was dried and then sublimed at 150°/0·05 mm. The red sublimate (m. p. 221—222°) of 3-methylalizarin was not further purified.

3-Methylalizarin 1-methyl ether. 3-Methylalizarin (1 g.) and boroacetic anhydride (2 g.) were refluxed in acetic anhydride (12 ml.) for 5 min., and the red solution left to cool. Next day the reddish-brown acetate–boroacetate was collected, washed with dry ether, and then decomposed by stirring it in cold water for several hours. The resulting *3-methylalizarin 2-acetate* was crystallised from alcohol (charcoal), forming long yellow needles, m. p. 196—197° (Found: C, 68·6; H, 4·1; Ac, 15·4. $C_{17}H_{12}O_5$ requires C, 68·9; H, 4·1; Ac, 14·5%). The above acetate (0·3 g.) in dry acetone (30 ml.) was refluxed with methyl iodide (2 ml.) and silver oxide (2 g.) for 11 hr., more methyl iodide (2 ml.) and silver oxide (2 g.) being added after 6 hr. After filtration and removal of the solvent, the residual *3-methylalizarin 2-acetate 1-methyl ether* was crystallised from alcohol, giving long yellow needles, m. p. 204° (Found: C, 69·4; H, 4·6. $C_{18}H_{14}O_5$ requires C, 69·7; H, 4·5%). Hydrolysis[3] of the ether acetate with methanolic potassium hydroxide afforded *3-methylalizarin 1-methyl ether* which crystallised from methanol in yellow needles, m. p. 219° not depressed on admixture with a sample of natural digitolutein, m. p. 218—219° (lit.,[3] corrected m. p. 222°) (Found: C, 71·5; H, 4·7. $C_{16}H_{12}O_4$ requires C, 71·6; H, 4·5%). The natural and synthetic materials had identical ultraviolet and infrared spectra.

We are indebted to Professor M.-M. Janot for a specimen of digitolutein, to Dr. H. F. Bondy for a sample of 3-methylcatechol, and to Dr. V. C. Farmer for the infrared spectra in potassium bromide discs.

THE UNIVERSITY, OLD ABERDEEN, SCOTLAND. [*Received, June 30th*, 1959.]

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840. *The Skraup Test for Pyridine-2-carboxylic Acids.*

By R. M. ACHESON and G. A. TAYLOR.

THE red colour produced by the interaction of solutions of ferrous salts with various pyridine-2-carboxylic acids was first observed by Skraup,[1] and was subsequently used as a test for this group of compounds. Ley *et al.*[2] prepared the complex ferrous salts of picolinic, pyrazine-3,5-dicarboxylic, and quinoxaline-2,3-dicarboxylic acid, all of which showed a low-intensity absorption maxima at *ca.* 5000 Å.

In order to put this test on a firmer basis the visible and ultraviolet absorption spectra of pyridine-mono- and -di-carboxylic acids in aqueous-methanolic ferrous ammonium sulphate were examined. All the acids with one carboxyl group adjacent to the nitrogen atom, and none of the others, gave a low-intensity absorption band in the region of 4000 Å. The absorption at longer wavelengths observed in the case of pyridine-2,6-dicarboxylic acid may be caused by this acid's acting as a terdentate ligand. Quinaldic acid and pyridine-2,4,5-tricarboxylic acid gave coloured solutions with the ferrous ammonium sulphate solution although no new maxima were observed. The colour is apparently caused by the broadening of the base of the normal absorption bands of the acids. Phenanthridine-6-carboxylic acid gave a purplish precipitate with the ferrous solution, and no colour was given by 2-methylimidazole-4,5-dicarboxylic acid. The maxima at 4400 Å and 5100 Å reported[3] for ferrous complexes of the type $[FeX_3]^-$ obtained from picolinic and quinaldic acid were not observed.

[1] Skraup, *Monatsh.*, 1886, **7**, 212.
[2] Ley, Schwarte, and Münnich, *Ber.*, 1924, **57**, 349.
[3] Shinra, Yoshikawa, Kato, and Nominzo, *J. Chem. Soc. Japan*, 1954, **75**, 44.

The extinction coefficients of the coloured species can only be evaluated if their composition and stability constants are known and so only the optical densities (O.D.) are recorded as a qualitative supplement to the test. Decreasing the pH of the picolinic

Absorption spectra of pyridine acids and their iron complexes.

Pyridine-carboxylic acid	$\lambda_{max.}$ (Å) ($\varepsilon \times 10^{-3}$) in aq. MeOH			Iron complexes		
	Alone	Acidified *	Basified †	Pyridine molality	$\lambda_{max.}$ (Å)	O.D.
-2-	2645 (5·2)	2645 (7·4)	2630 (0·87)	$4{\cdot}79 \times 10^{-4}$	3980	0·66
	2125 (5·9)	2100 (4·1)				
-3-	2625 (3·6)	2635 (4·9)	2625 (3·0)			
	2120 (6·6)	2170 (4·9)				
-4-	2610 (3·3)	2700 (4·4)	2665 (2·3)			
	2130 (6·0)	2175 (6·4)				
-2,3-	2740 (3·7)	2680 (4·1)	2685 (3·3)	$5{\cdot}17 \times 10^{-4}$	3990	0·66
-2,4-	2580 (2·3)	2600 (3·0)	2595 (1·9)	$3{\cdot}68 \times 10^{-4}$	4100	0·18
	2190 (4·3)	2220 (3·4)				
-2,5-	2725 (7·1)	2700 (7·6)	2700 (6·0)	$3{\cdot}07 \times 10^{-4}$	4141	0·31
	2230 (9·25)	2260 (9·1)				
-2,6-	2700 (6·1)	2705 (4·45)	2700 (4·4)	$4{\cdot}36 \times 10^{-4}$	4612	0·81
	2190 (7·1)	2235 (7·4)				
-3,4-	2635 (3·7)	2615 (4·6)	2645 (2·5)			
-3,5-	2685 (3·0)	2660 (3·8)	2690 (2·7)			
		2180 (8·6)				
-2,4,5-	2750 (1·1)	2760 (1·1)	2720 (0·89)			

* With sulphuric acid. † With sodium hydroxide.

acid–ferrous ammonium sulphate solution mentioned in the Table from 4·6 to 1·4 by the use of a hydrochloric acid–sodium acetate buffer caused the optical density of the solution to drop from 0·66 to 0·02 at the wavelength of maximum absorption. The position of the maximum was unaltered.

Experimental.—Ultraviolet absorption spectra were measured on a Cary recording spectrophotometer. The acids were examined in water containing methanol (10% v/v). The coloured complexes were produced by adding freshly prepared aqueous ferrous ammonium sulphate hexahydrate (0·5 ml. of 0·174M) to the pyridine-acid in 50% aqueous methanol (10 ml.), and the optical densities of the resulting solutions were measured in 4 cm. cells.

We thank Mr. A. O. Plunkett for technical assistance, Dr. D. G. Wibberley for the gift of pyridine-2,4,5-tricarboxylic acid,[4] and the Department of Scientific and Industrial Research for a maintenance grant (to G. A. T.).

Department of Biochemistry, Oxford University. [*Received, July 1st*, 1959.]

[4] Tittensor and Wibberley, *J.*, 1958, 3161.

XUM

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ERRATA

Vol. 1954, page 410, line 14*. *For* (ε 9,700) *read* (ε 9,300).
Line 13*. *For* (ε 19,600) *read* (ε 18,500); *for* (ε 23,700) *read* (ε 22,900).
Line 8*. *For* (ε 11,000) *read* (ε 8,100).
Line 7*. *For* (ε 21,000) *read* (ε 15,700).
Line 2*. *For* (ε 10,600) *read* (ε 6,400); *for* (ε 20,600) *read* (ε 13,400).

Vol. 1954, page 411, line 1. *For* (ε 11,500) *read* (ε 5,800); *for* (ε 25,800) *read* (ε 12,900).
Line 2. *For* (ε 8,400) *read* (ε 6,000); *for* (ε 14,500) *read* (ε 10,500).
Line 12. *For* (ε 17,400) *read* (ε 12,900).
Line 17. *For* (ε 16,800) *read* (ε 12,200); *for* (ε 26,400) *read* (ε 20,000).

Vol. 1956, page 4844, Figure 1 shows the relative positions of the ions in the crystal plane incorrectly and should be replaced by the accompanying Figure.

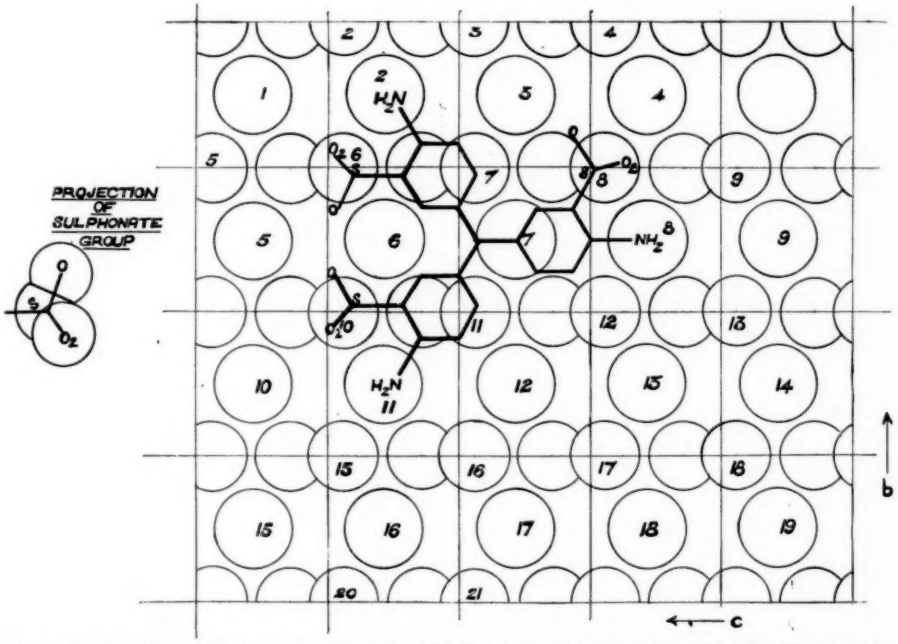

Figure 2 shows the nitrate ions as apparently similarly disposed in the plane. The Figure should be interpreted as an arrangement of the ions with alternate rows as near reflections of one another in (001) but with glides of half the *a* primitive translation.

Vol. 1958, page 168, line 12. *Right hand side should read*

$$Br{\cdot}C_6H_4{\cdot} + PhNO_2 \longrightarrow p\text{-}Br{\cdot}C_6H_4{\cdot}C_6H_4{\cdot}NO_2 \ (o, m, p)$$

Vol. 1958, page 3504, formula (I). *For* Pr *read* COEt.

Vol. 1959, page 589, lines 20* and 19*. *For* C1 *read* 1C.
Line 20*. *For* 1C *read* C1.

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* From bottom of main text.

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Errata.

Vol. 1959, page 1056, line 27. *For* $k_{Hg-C} = 2{\cdot}61 \times 10^{-5}$ *read* $k_{Hg-C} = 2{\cdot}61 \times 10^{5}$.

Vol. 1959, page 2030, equation (4). *Should read* $L_1/L = [(p_L/p_0)^2 - 1]/[(p_1/p_0)^2 - 1]$.

Vol. 1959, page 2199, Table. *Interchange* (I) *and* (II).

Vol. 1959, page 2365, line 19*. For N-2-*cyano*-4-*nitrophenyl*-N-*methylhydrazine* read-*amino*-1-*methyl*-5-*nitroindazole*.

Vol. 1959, page 3025, footnote *. *For* 1948 *read* 1958.

Vol. 1959, page 3106, Table 4, column 1. *For* 1·1 (19·0°) *read* 11 (19·0°).

Vol. 1959, page 3109, lower Table, second column. *For* 0·26 *read* 2·6.

* From bottom of main text.

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